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Dissertation

Method development for continuous monitoring of selected VOC test gases by GC and SIFT-MS and its use for verifying a new dosing system for test gas generation

Vorgelegt von
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Kurzfassung

Im Bereich des Arbeits- und Gesundheitsschutzes sind Gefahrstoffmessungen einer der Eckpfeiler bei der Prävention von Berufskrankheiten. Das Institut für Arbeitsschutz (IFA) entwickelt und publiziert Methoden für die Messung von Gefahrstoffen und führt die Gefahrstoffanalysen für die Unfallversicherungsträger auch selber durch.

Analytische Methoden verändern sich mit der Zeit aufgrund von technischem Fortschritt und sinkenden Grenzwerten. Im Rahmen der Methodenentwicklung werden im IFA Messverfahren unter Einflussgrößen wie Luftfeuchte und Temperatur an dynamischen Prüfgasatmosphären getestet. Diese Prüfgase müssen hohe Anforderungen hinsichtlich Richtigkeit, Homogenität, Präzision und Stabilität erfüllen, vor allem, wenn, wie im IFA, das generierte Prüfgas auch für Ringversuche verwendet wird.

Diese Arbeit beschäftigt sich zum einem mit der selektiven, quantitativen online-Analytik dynamischer Prüfgase und zum anderen mit der Prüfgasherstellung von Substanzen mit hohem Dampfdruck und niedrigen Siedepunkten.

Um die Qualität des Prüfgases online sicherstellen zu können, wurden zwei Messsysteme zur online Überwachung in den Prozess der Prüfgasherstellung integriert. Auf einem online-Gaschromatograph (GC) und einem direktanzeigenden Massenspektrometer wurden verschiedene Methoden entwickelt, um unterschiedliche Prüfgase in Hinblick auf Konzentrationsbereich und Substanzklasse selektiv analysieren zu können.

Auf dem online-GC wurden Methoden für die Analyse der sogenannten flüchtigen organischen Verbindungen (VOC) entwickelt. Eine Methode bestimmt die Analyten im µg/m³ Bereich, so wie sie üblicherweise an Innenraumarbeitsplätzen vorkommen. Die zweite Methode ist für die Analyse von flüchtigen organischen Verbindungen im mg/m³ Bereich ausgelegt, wie sie typischerweise an Arbeitsplätzen bei Tätigkeiten mit organischen Lösemitteln vorkommen. Die entwickelten Methoden liefern ca. alle 7 – 15 Minuten ein Ergebnis, das alle Anforderungen hinsichtlich Wiederfindung, Bestimmungsgrenze, Präzision und Richtigkeit erfüllt. Um die quantitative Prüfgaszusammensetzungen in wenigen Sekunden zu messen, wird ein Selected Ion Flow Tube Mass Spectrometer (SIFT-MS) genutzt. Auch auf dieser Technik werden Analysenmethoden für verschiedenen Substanzklassen etabliert. So lässt sich ebenfalls die quantitative Zusammensetzung der VOC Prüfgase mittels SIFT-MS mit guter Qualität ermitteln. Besonders geeignet ist die Technik, um das Einlaufverhalten von Prüfgasen oder kurzfristige Veränderungen in der Prüfgaszusammensetzung zu überwachen.

Der zweite Teil dieser Arbeit befasst sich mit der Prüfgasherstellung von Substanzen mit hohem Dampfdruck und niedrigen Siedepunkten am Beispiel der kurzkettigen Aldehyde. Die besondere Herausforderung dabei ist, dass die gesamte Dosierung in einer gekühlten Umgebung durchzuführen ist, um das Ausgasen, der Aldehyde in den Leitungen zu vermeiden. Es wurde durch Kombination dreier

Einzelkomponenten ein neuartiges System zur Generierung von Prüfgasen entwickelt. Das System ist modular aus einer Mikrodruckpumpe, einer hochpräzisen Kühleinheit sowie einem modifizierten gaschromatographischen Verdampfungssystem zusammengesetzt und ist geeignet, Aldehydprüfgase mit der geforderten Qualität in der dynamischen Prüfgasstrecke des IFA herzustellen. Die Eignung des Systems konnte durch paralleles Untersuchen mittels SIFT-MS und klassischer HPLC offline Analytik erfolgreich gezeigt werden.

Abstract

In the field of occupational health and safety, the measurement of hazardous substances is one of the cornerstones in the prevention of occupational diseases. The Institute for Occupational Safety and Health (IFA) develops and publishes methods for the measurement of hazardous substances and also carries out the hazardous substance analyses for the accident insurance companies.

Analytical methods change over time due to technical progress and decreasing limit values. Within the framework of method development, IFA tests measurement procedures under influencing variables such as humidity and temperature in dynamic test gas atmospheres. These test gases have to meet high requirements regarding correctness, homogeneity, precision and stability, especially if, as at IFA, the generated test gas is also used for proficiency tests.

This work deals on the one hand with the selective, quantitative online analysis of dynamic test gases and on the other hand with the test gas generation of substances with high vapor pressure and low boiling points.

To ensure the quality of the test gas online, two measuring systems for online monitoring were integrated into the process of test gas generation. Different methods were developed on an online gas chromatograph (GC) and a direct-reading mass spectrometer to selectively analyze different test gases with regard to concentration range and substance class.

For the online-GC, methods for the analysis of the so-called volatile organic compounds (VOC) were developed. One method determines the analytes as they usually occur at indoor workplaces in the µg/m³ range. The second method is designed for the analysis of volatile organic compounds in the mg/m³ range, as they typically occur at workplaces where organic solvents are used. The developing methods deliver a result approximately every 7 - 15 minutes, which fulfills all requirements regarding recovery, limit of quantification, precision and accuracy. A Selected Ion Flow Tube Mass Spectrometer (SIFT-MS) is used to measure the quantitative test gas compositions in real time. Analytical methods for different substance classes are also established with this technique. Thus, the quantitative composition of the VOC test gases can also be determined with good quality using SIFT-MS. The technique is particularly suitable for monitoring the equilibration phase of test gases or short-term changes in the test gas composition.

The second part of this thesis deals with the test gas production of substances with high vapor pressure and low boiling points using the example of short-chain aldehydes. The special challenge here is that the entire dosage has to be carried out in a cooled environment to avoid outgassing of the aldehydes in the tubing. By combining three individual components, a novel system for generating test gases was developed. The system is modularly composed of a micro pressure pump, a high precision cooling unit and a modified gas chromatographic evaporation system. It is suitable to produce aldehyde test gases with the required quality in the dynamic test gas facility of the IFA. The suitability of the system was successfully demonstrated by parallel investigations using SIFT-MS and classical offline-HPLC analysis.

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1 Introduction

The assessment of air quality is of interest in many fields. As varied as these areas of interest are, so different are the air pollutants of concern. For example, the team around atmospheric researcher J. Lelieveld and cardiologist T. Münzel published a study in 2019 according to which about 120 people per 100,000 inhabitants worldwide die prematurely every year as a result of polluted air. [1] Both, in this study and in the field of air quality research in general, particulate matter is of major interest. Airborne contaminants are identified as the main cause of respiratory and cardiovascular diseases. Another field of interest is atmospheric research, which investigates and elucidates atmospheric chemical processes, among other aspects. Examples are the formation of smog and acid rain and probably the most prominent phenomenon: the hole in the ozone layer over the Antarctic continent and the chlorofluorocarbons involved in it. This research area thus makes important contributions to the understanding of the earth's climate. For this purpose, researchers use different methods. In addition to statistical models, field measurements and laboratory studies, emission measurements in atmospheric chemistry are of great importance. Related research areas are environmental chemistry and environmental technology, for which the measurement of air pollutants is also of significant interest. All research areas dealing with air contamination, whether in the atmosphere, in open air, indoors or at workplaces, have in common that suitable analytical instruments and methods must be available to quantify air pollutants.

In occupational health and safety, it is not primarily a question of conducting academic research, collecting data or clarifying chemical processes, but rather protecting people from exposure to known pollutants in workplace air. Emission measurement is one of the cornerstones in prevention against occupational diseases. After all, many activities in the workplace require the handling of hazardous chemical substances. These include all substances or mixtures whose production or use can be expected to have a damaging effect on humans. The German Ordinance on Hazardous Substances (GefStoffV) of 26.11.2010 defines the term in § 2 paragraph 1 and 2 even more extensively. [2] In particular, employees in the industrial sector like the chemical industry, metal industry or mining industry are exposed to a wide variety of hazardous substances. According to the German Institute for Occupational Safety and Health (IFA), health complaints at indoor workplaces such as offices or classrooms are often also directly related to the occurrence of hazardous substances in the air. Classical examples are formaldehyde or wood preservatives. According to § 7 of the German Ordinance on Hazardous Substances, when dealing with hazardous substances or exposure to them in general, the employer is obliged to determine and assess the extent, type and duration of inhalation exposure. [3] The determination and assessment of these exposures in the air of the work area is carried out in accordance with the Technical Rules for Hazardous Substances (TRGS) 402, "Determination and Assessment of Hazards during Work with Hazardous Substances: Inhalative exposure". [4] The binding assessment criterion is compliance with the Occupational Exposure Limits (OELs) for hazardous substances. These limits are published in the TRGS 900 [5] and for carcinogenic compound in the TRGS 910 [6]. For non-carcinogens, compliance with the occupational exposure limit values serves to protect the health of employees from the risk of inhalation of substances. [5] For carcinogens, the limit values are derived from a risk-based concept with the target that compliance with this limit will cause a similar risk to get a work-related cancer comparable to the normal life-risk [6].

Detailed requirements for the assessment of workplaces are published in the Annex 1 of TRGS 402, DIN EN 689 as well as DIN EN ISO/IEC 17025. [7,8,9] In Germany, the employer has to ensure that the workplaces comply with the requirements. If he himself does not have the necessary competence, accredited external measuring institutes can be commissioned with this task. Valid measuring methods and sampling procedures are necessary tools for workplace assessment.

As part of the accreditation procedure, the measuring institutions must document their laboratories' suitability. In order to prove this, quality assurance measures (including proficiency tests) must be carried out and documented in accordance with the requirements. IFA`s proficiency testing scheme is recommended as suitable by the *Deutsche Akkreditierungsstelle* (DAkkS). IFA has been an established provider of international proficiency tests for many years since 1989 [10]. In addition, IFA offers the measuring institutions support in various areas. For example, in the provision of specialized information and expert knowledge, IFA provides training courses on various topics such as direct reading measuring devices and sampling techniques and advice on operational measurements. Furthermore, the IFA is part of the "Measuring System for Risk Assessment of Accident Insurance Institutions" MGU [11], which offers information on hazardous substances in databases (e. g. GESTIS Hazardous Substances Database, GESTIS – International limit values) [12], develops and publishes measuring methods for the analysis of hazardous substances and of course carries out the hazardous substance analyses itself.

1.1 State of the art

Although measurements of hazardous substances in workplace air have been carried out for decades, the development of measurement methods is still an important research focus. Analytical methods change over time due to technical progress and decreasing OELs. Apart from very few exceptions, OELs are defined exclusively for the air in the workplace. Workplace air is, therefore, a primary prerequisite and must always be taken into account when developing new methods. For gases and vapors, suitable test atmospheres entail the highest level of workplace air simulation. The generation of test gas atmospheres is a complex process. Certainly, there are also possibilities to produce standards for method development that require less equipment than the production of a test gas, e.g. dosing the analyte in liquid form onto the sample carrier or using commercial gas standards. Nevertheless, the production of a test gas offers more flexibility; e.g. in concentration, composition and volume of the gas is mentioned as the preferred method in the regulations and standardization for the development of measuring methods [13]. Parameters for sampling can be determined best in this way and influencing variables such as humidity and temperature can be included in the method development.

Since IFA offers the proficiency tests described in this thesis with sampling for up to thirteen participants, a correspondingly large amount of test gas must be provided. Therefore, the production of dynamic test gases from pure substances is the method of choice. These test gases are generated in the so-called test gas facility. The dosed and vaporized analytes are introduced continuously into a basic gas stream and conditioned. Depending on the substance class and desired concentration, different dosing and vaporization techniques are used. For the production of test gases of thermally stable substances with a high vapor pressure, an automatic calibration gas generator is used, which generates test gases in the mg/m³ down to the low µg/m³ range at air flow rates from 1 to 6 m³/h in the test gas facility. The test gases generated in this way meet all requirements regarding accuracy, homogeneity, precision and stability, so that they have been used successfully in proficiency tests for many years. The technology used corresponds to the state of the art. The system is not suitable for the generation of aldehyde test gases due to their high vapor pressure. Especially acetaldehyde, with a boiling point close to room temperature, can only be precisely dosed from a cooled environment. The aldehydes investigated during the work on this thesis are (besides acetaldehyde): formaldehyde, propionaldehyde and butyraldehyde. Acetaldehyde, propionaldehyde and butyraldehyde are dosed as methanolic solution into a cooled chamber via a syringe feeder. Methanol is used to increase the volume because the amount of pure substance to be dosed is too small to achieve a stable desired concentration in the test gas (at 4 m³/h) with the dosing range of the syringe feeder. Furthermore, methanol does not interfere with the subsequent analysis. Formaldehyde is obtained by permeation of paraformaldehyde. This method, too, has been tried and tested for years. It fulfils all the requirements already mentioned and is still state-of-the-art. Prepared test gases must be monitored continuously. The possibilities for monitoring the test gases during production and sampling are limited to the use of a flame ionization detector and an older gas chromatographic system that is not suitable for high-resolution analysis and trace analysis. Therefore, the determination of the quantitative composition of the test gas is done afterwards by analyzing the sample carriers.

1.2 Objective

In view of the upcoming relocation of the test gas facility to a new building, a new facility with greater capacity is to be purchased. In the course of this, due to the limited possibilities for online monitoring, analytical equipment for online control of the test gases for high-resolution analysis and trace analysis is to be selected and purchased, on which appropriate methods for selective and quantitative determination of the generated test gases can be created. For this purpose, two different systems have been purchased: an online gas chromatograph and a direct reading mass spectrometer. On the online-GC, methods for the analysis of the volatile organic compounds (VOC) are developed. One method determines the analytes in the µg/m³ range as they usually occur in indoor workplaces. The second method is for the analysis of test gases of this substance class in the mg/m³ range. The concentration range is based on workplace limits and is found at this level in workplaces where organic solvents are used. Therefore, in this thesis, a distinction is made between VOC test gases and organic solvents test gases and proficiency tests, respectively, although they are mostly the same substances. The difference in the naming refers only to the concentration of the selected substances. The online methods to be developed should be as fast as possible and still be on the level of an offline analysis regarding recovery, limit of quantification, precision and accuracy.

Aldehyde test gases cannot be monitored with the online-GC. For the quantitative determination of this substance class, a selected ion flow tube mass spectrometer (SIFT-MS) is used. With this technique, the quantitative test gas composition can be measured in a few seconds and can, therefore, be considered as a direct reading analyzer. The measurement of VOC test gases is also possible with SIFT-MS. Methods for the measurement of aldehyde test gases and VOC test gases are developed and their suitability is finally tested for quality control in proficiency tests. In addition to the routine use during a proficiency test, independent online analysis is necessary for the development of sampling methods. Notably the SIFT technique offers numerous and various new substances to be monitored and extents the options for the test gas facility.

The second part of this thesis deals with the production of test gases for substances with low boiling points and high vapor pressure. As first substances aldehydes were selected, which are used in the proficiency test. The aim of selection was also to remove methanol from the test gas. Therefore, a novel system for the test gas generation is developed using a combination of three components:

- A microfluidic pressure pump system for precise dosing of smallest dosing rates.
- A cooling unit for temperature control of the flow path to prevent bubble formation in the flow path for consistent transport of the compounds.
- An evaporator for generation of pulsation-free vapor mixtures.

2 Motivation and theoretical background

2.1 Proficiency testing at the IFA

Proficiency testing as a key method for external quality control enables laboratories to monitor their performance and compare their results with similar laboratories. For that reason, the IFA has been providing proficiency test schemes on various hazardous substances in workplace environments since 1989 [10,14,15,16,17,18]. Current substance groups for proficiency testing are volatile organic compounds, organic solvents, aldehydes, inorganic acids and metals in dust. Except for metals in dust, the provided test gas for proficiency testing is generated at IFA´s dynamic test gas facility (Detailed description of test gas generation is given in Chapter 3.1).

Participants can choose two options:

- Ordering samples prepared by IFA, or
- Alternatively, participants perform on site sampling with their own equipment.

On site sampling takes a possible factor of the individual sampling equipment and sampling procedure as a source of error into account. Measuring methods for VOCs and solvents have to be screening methods with a wide variety of different organic substances from non-polar alkanes to polar compounds like esters. For this reason, the basic measurement methods for, e.g., organic solvents used at workplaces or organic compound that can appear at so-called “indoor workplaces” like offices, have to cover a range of compounds as wide as possible. As a consequence, the proficiency testing programs for VOC´s and organic solvents have mostly the same analytes. The difference is primarily in the concentration range. The concentration of organic solvents in the related proficiency test refers to the occupational exposure limit OEL [5]. The concentration for each individual substance is between 0.01 and two times OEL (for instance methanol: OEL is 270 mg/m^3, leads to a concentration range during proficiency testing from 2.7 to 540 mg/m^3). The concentration of the VOC´s whereas are based on the indoor workplace reference values of various VOCs [19,20]. The concentration range for each individual VOC during proficiency tests is therefore fixed from 10 to 200 µg/m^3. Furthermore, the low acceptance concentration of 200 µg/m^3, which is specified for benzene in the exposure risk assessment, enables this compound to be introduced in the VOC proficiency testing scheme. [6]

For the aldehyde proficiency test, test gas mixtures with different concentrations of individual substances are accessible. The aldehydes used for proficiency testing are formaldehyde, acetaldehyde, propionaldehyde and butyraldehyde. The concentrations of acetaldehyde, propionaldehyde and butyraldehyde in the test gases range from 0.1 and 3 mg/m^3 and for formaldehyde from 0.03 to 1.0 mg/m^3, respectively. This is based on the occupational exposure limit value of 0.37 mg/m^3. [6]

2.2 Selected ion flow tube mass spectrometry

Selected Ion Flow Tube Mass Spectrometry (SIFT-MS) is a form of direct mass spectrometry. It offers the ability of simultaneous real-time quantification of several trace gases, e.g., in whole air samples. It utilizes precisely controlled chemical ionization reactions to detect and quantify the VOC analytes. It relies on chemical ionization of the trace gas molecules in air samples introduced into helium as carrier gas, using different reagent ions (most commonly, H_3O^+, NO^+ and O_2^+). The reagent ions react with the trace compounds in air, but do not react with air itself. Reactions between the reagent ions and the trace gas molecules proceed for an accurately defined time, the reagent and product ions being detected and counted by a downstream mass spectrometer. Absolute concentrations of trace gases in air can be determined by SIFT-MS down to parts-per-trillion (ppt) levels. Sample preparation or separation of the compounds is for most applications not required. Calibration using chemical standards is also not required, as the concentrations are calculated using the known reaction rate constants and measured flow rates and pressures. [21]

Flowing afterglow and SIFT techniques have provided valuable insights into the ion molecule reactions occurring in earth’s ionosphere and interstellar clouds. In particular, these techniques were used to determine the rate coefficients and products of reactions between ions and molecules in the gas phase [22, 23, 24]. Before SIFT-MS became a commercialized technique, researchers had focused on using Flowing Afterglow and later SIFT to define rate constants. [25, 26, 27, 28, 29, 30, 31, 32] A review article on SIFT and the SIFT-MS technique was published in 2005. This review contains an evaluation of the literature in this area. [33] Subsequently, those known rate coefficients are used to determine the concentration of target compounds, and this application technique is denoted SIFT-MS [34]. A library of SIFT-MS reactions, including the rate constants and product ion masses, has been developed and these have enabled SIFT-MS to be used as an accurate analytical method for quantification of trace gases in whole air samples. The primary advantage of SIFT-based techniques in trace gas analysis is the speed of response. Compared to methods solely reliant on electron impact ionization, chemical ionization of the analyte is a relatively soft ionization process that yields greatly simplified mass spectra. This means that no chromatographic separation is required to analyze trace gases in real time. [35]

2.2.1 Operating principles of the SIFT-MS technique

A SIFT-MS instrument consists of three distinct regions. Figure 1 gives a graphical overview.

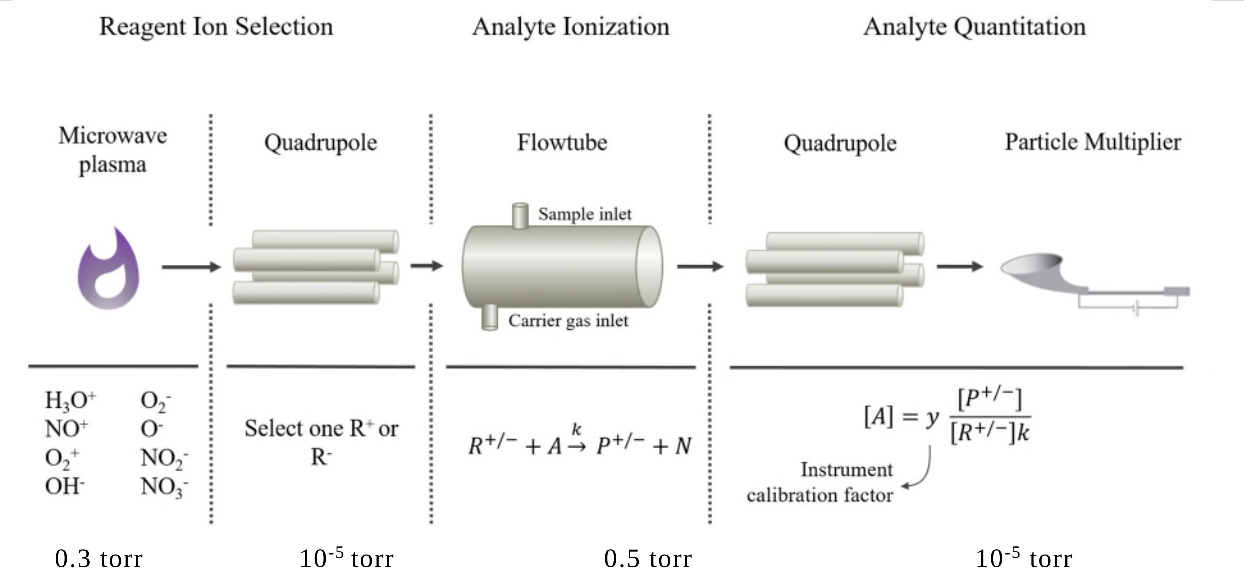


Figure 1: Operational principles of the SIFT-MS technique. [36]

2.2.1.1 Reagent ion selection

Reagent ions are selected from a mixture of ions generated by a microwave plasma through moist air. The first quadrupole mass filter (Upstream chamber) of the instrument selects reagent ions of a given mass-to-charge ratio. The generable reagent ions are H_3O^+, NO^+, O_2^+, O^-, O_2^-, OH^- NO_2^- and NO_3^-. These ions react with most organic molecules but do not react with the major constituents of ambient air. Switching of reagent ions happens in ten milliseconds. [37]

2.2.1.2 VOC ionization

Here carefully controlled ion-molecule reactions take place. These reactions occur when the preselected reagent ion ionizes the reactive compounds in the sample. The reaction chamber is a flow tube. The selected reagent ions are drawn into the flow tube by a helium carrier gas flow. The sample gas rate is known via a calibrated flow restrictor inlet. Before the sample molecules are transported into the reaction region of the flow tube they are cooled down by the carrier gas to a consistent temperature. This leads to reproducible ion chemistry, which allows, inter alia, the use of an MS library. After that, the reagent ions react with the sample molecules via different ion-molecule reaction pathways and predictable product ions are formed. [37]

2.2.1.3 VOC quantification

In region 3 the product ions and unreacted reagent ions are sampled by the second quadrupole mass filter (Downstream chamber) and a particle multiplier detector measures the count rate at selected masses. Software processes these data, together with instrumental parameters, to calculate absolute concentrations of target compounds, in real time. The linear range of quantitation of VOCs is typically from mid-pptv to tens of ppmv, but can be extended to the percentage range by restricting the flow of sample into the instrument or by diluting the sample prior to analysis. [37]

2.2.2 Measurement principle of SIFT-MS

Before the quantification and reaction mechanisms of a SIFT-MS measurement technique are explained in detail, an overview of the background of the measurement technique is given and important terms are explained.

Whereas the conventional approach to preform quantitative measurements is to construct a calibration curve using known-concentrations samples, SIFT-MS delivers quantitation without calibration if the kinetics of the target compound are known. This is achieved by the two main features of the SIFT-MS technique. First, the pure reagent ion delivery and real-time switching of the reagent ions and secondly a predictable reaction chemistry in the flow tube. Real-time switching (ten milliseconds) of reagent ions means all ions can be used in a single analysis of the sample by using the quadrupole. The predictable reaction chemistry is achieved by consistent reagent ion energy, which is a critical factor in controlling analyte ionization. Controlled analytical ionization leads to very consistent product ion formation and accordingly enables reliable and stable quantification. To obtain controlled ionization, the carrier gas thermalizes the reagent ions before they encounter the sample, which means that the energies of the reagent ions are as low and uniform as possible, see Figure 2. The resulting sharp reagent ion energy distribution enables predictable, precise and ultra-smooth chemical ionization. [36][38]

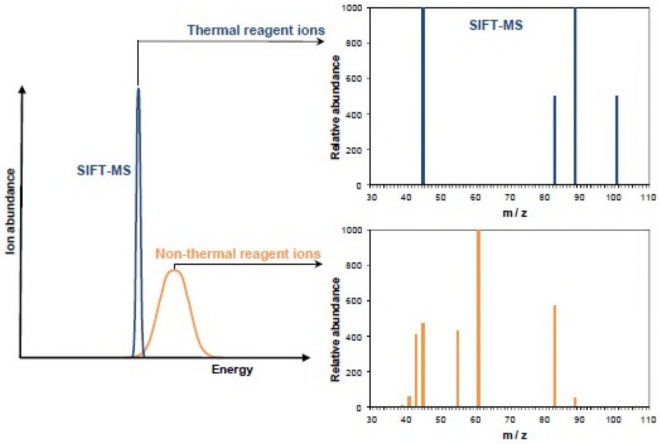


Figure 2: Schematic diagram illustrating the different reagent ion energy distributions in SIFT-MS and other chemical ionization mass spectrometers. [38]

As mentioned before, concentrations are calculated using known reaction rate constants of the different ion-molecule reaction pathways between the analyte and the available reagent ions. The reaction rate describes the collisions of the compound molecule with the reagent ion that result in a reaction to form product ions. The reaction efficiency is from 0% (that is, no reaction) to 100 %, a very efficient, fast reaction where every collision between the reagent ion and the molecule leads to a reaction ($k \approx k_{coll}$). The collision rate k_{coll} is the rate at which a specific ion and molecule will collide per second in a specific volume of gas.

The collision rate can be calculated theoretically based on the dipole moment and the polarizability of the molecule. A faster reaction results in more product ions being formed and provides a higher sensitivity than a slower reaction. For a given compound, the reaction rates vary between the reagent ions being used; see Table 1 below. [36] [1]

Table 1: Reaction rates of acetaldehyde with different reagent ions. [36]

Reagent ion	Collision rate k_{coll} [cm^3 $molecule^{-1}$ s^{-1}]	Reaction rate k [cm^3 $molecule^{-1}$ s^{-1}]
H_3O^+	$3.7E^{-9}$	$3.7E^{-9}$
NO^+	$3.2E^{-9}$	$0.6E^{-9}$
O_2^+	$3.1E^{-9}$	$2.3E^{-9}$

The reaction rates of the compounds with the different reagent ions can be found in the SIFT-MS library and are either experimentally determined or theoretically calculated.

However, an ion-molecule reaction does not always lead to just one product, but some reactions have multiple product channels. The ratio of the product channels to the total product signal for that reagent ion is called the branching ratio (BR). As an example, the library entry of acetone is shown in the figure below. As can be seen, the branching ratio of the dissociative electron transfer product (m/z 43) by example is 0.4. [39]

Table 2: Library entry of acetone in the SIFT-MS compound library [39]. Green highlights the dissociative electron transfer product of O_2^+ with acetone. Red highlights secondary chemistry products of H_3O^+.

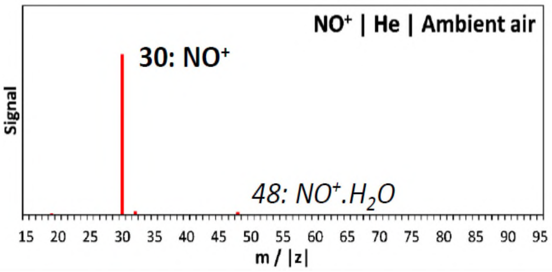
Compound	Reagent ion	Reaction rate k [cm^3 $molecule^{-1}$ s^{-1}]	Branching ratio [%]	Mass (m/z)	Product
Acetone	H_3O^+	$3.9E^{-9}$	100	59	$C_3H_7O^+$
	H_3O^+	$3.9E^{-9}$		77	$(CH_3)_2CO{\bullet}H^+{\bullet}H_2O$
	H_3O^+	$3.9E^{-9}$		117	$((CH_3)_2CO)_2{\bullet}H^+$
	NO^+	$1.2E^{-9}$	100	88	$NO^+{\bullet}C_3H_6O$
	O_2^+	$2.7E^{-9}$	40	43	$C_2H_3O^+$
	O_2^+	$2.7E^{-9}$	60	58	$C_3H_6O^+$

What also emerges from Table 2 is that some products (highlighted in red) are not assigned branching ratios. This is always the case when secondary chemistry is involved. By definition, it is primary chemistry when the initial reagent ion reacts directly with the target molecule to form a product. Secondary chemistry, whereas, arises from reactions between ions and other high-concentration molecules, for example water (most common), carbon dioxide (negatively charged ions) or oxygenated VOCs. Secondary chemistry often occurs via the association mechanism. Association occurs with both positive and negative reagent ions.

There are two different types of secondary chemistry to pay attention to while using SIFT-MS: secondary chemistry of the reagent ions and of the product ion formation. Figure 3 shows the spectra of some reagent ions in moist sample conditions on a helium instrument with their respective secondary chemistry. [40]

---

[1] The notation used for the reaction rate conforms to the scientific format and displays a number in exponential notation, replacing part of the number with E^{-n}, where E multiplies the previous number by 10 to the n^th power.



Reagent ion secondary reactions:

$NO^+ + H_2O + M \rightarrow NO^+{\cdot}H_2O + M$

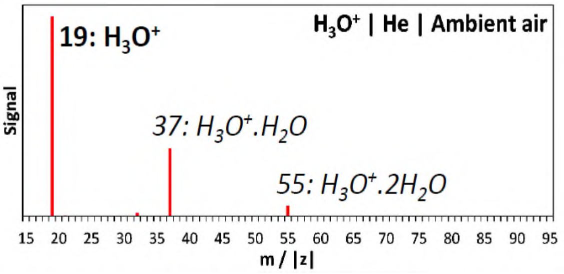
(m/z = 30) (m/z = 48)

$NO^+{\cdot}H_2O + H_2O + M \rightarrow NO^+{\cdot}2H_2O + M$

(m/z=48) (m/z = 66)

Secondary reagent ion formation: Very slow
Secondary reagent ion reactivity: Very low

OVERALL IMPACT: VERY LOW



Reagent ion secondary reactions:

$H_3O^+ + H_2O + M \rightarrow H_3O^+{\cdot}H_2O + M$

(m/z = 19) (m/z = 37)

$H_3O^+{\cdot}H_2O + H_2O + M \rightarrow H_3O^+{\cdot}2H_2O + M$

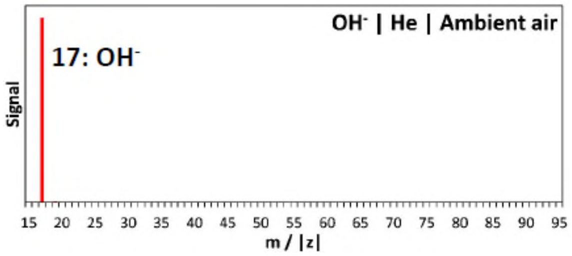
(m/z = 37) (m/z = 55)

$H_3O^+{\cdot}2H_2O + H_2O + M \rightarrow H_3O^+{\cdot}3H_2O + M$

(m/z = 55) (m/z = 73)

Secondary reagent ion formation:
Slow
Secondary reagent ion reactivity:
37: Moderate; 55 Low; 73 Very low

OVERALL IMPACT: MODERATE



Reagent ion secondary reactions:

$OH^- + H_2O + M \rightarrow OH^-{\cdot}H_2O + M$

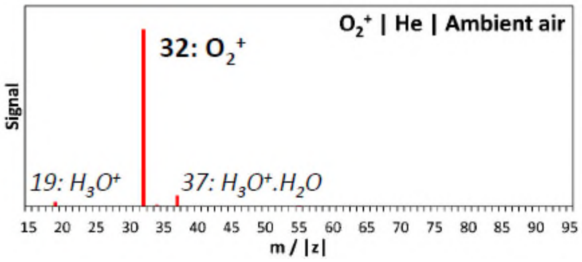
(m/z = -17) (m/z = -35)

$OH^- + CO_2 + M \rightarrow OH^-{\cdot}CO_2 + M$

(m/z = -17) (m/z = -61)

Secondary reagent ion formation:
-35: Very slow; -61 Moderate
Secondary reagent ion reactivity:
Very low

OVERALL IMPACT: LOW



Reagent ion secondary reactions:

$O_2^+ + H_2O + M \rightarrow O_2^+{\cdot}H_2O + M$

(m/z = 32) (m/z = 50)

$O_2^+ + \ldots\ldots \rightarrow H_3O^+ H_2O + \ldots\ldots$

(m/z = 50) (m/z = 37)

$H_3O^+{\cdot}H_2O + H_2O + M \rightarrow H_3O^+{\cdot}2H_2O + M$

(m/z = 37) (m/z = 55)

Secondary reagent ion formation:
50: Extremely slow; 19, 37: Moderate
Secondary reagent ion reactivity:
37: Moderate; 55 Low; 73 Very low

OVERALL IMPACT: MODERATE

Figure 3: Secondary Chemistry of H_3O^+, NO^+, OH^- and O_2^+ reagent ions in moist sample conditions [40]

The water clusters of the reagent ion can have significant effects on the reported concentration in highly humid samples. The secondary reactions of O_2^+ leading to H_3O^+ ions in the O_2^+ spectrum are not fully understood. Possible secondary products resulting from these secondary reactions cannot be assigned to the O_2^+ signal. Thus, quantification via O_2^+ at high humidity could be problematic if no calibration at the corresponding humidity is performed. Heating the flow tube mitigates these effects significantly. [40]

In terms of product ions, there are two product ion types: primary product ions and secondary product ions. Usually, concentrations can be determined using a subset of reaction products. Primary product ions arise from reactions between the analyte and the reagent ions. They have well defined branching ratios (relative signal levels). Not all primary products need to be measured to perform a quantitative analysis. Syft instruments calculate concentrations of the different reaction channels independently and compare them. A detailed description of the quantification process is given in the next chapter. [40]

Secondary products arise from reactions between product ions and other high-concentration molecules, such as water. Each secondary product has an associated primary product from which it was derived. The set of all secondary products together with the associated primary product ion is a reaction channel (see Figure 4). To perform quantitative measurements, all products in a reaction channel must be measured. The result of the channel is the sum of concentrations determined from primary and secondary ions. [40]

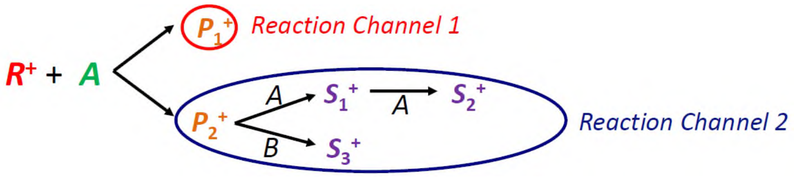


Figure 4: Reaction channels for quantitative analysis in SIFT-MS. [40]

To give a practical example on that, in Figure 5 the reactions showing the chemical mechanism of acetone are displayed, with the respective mass spectra underneath in Figure 6.

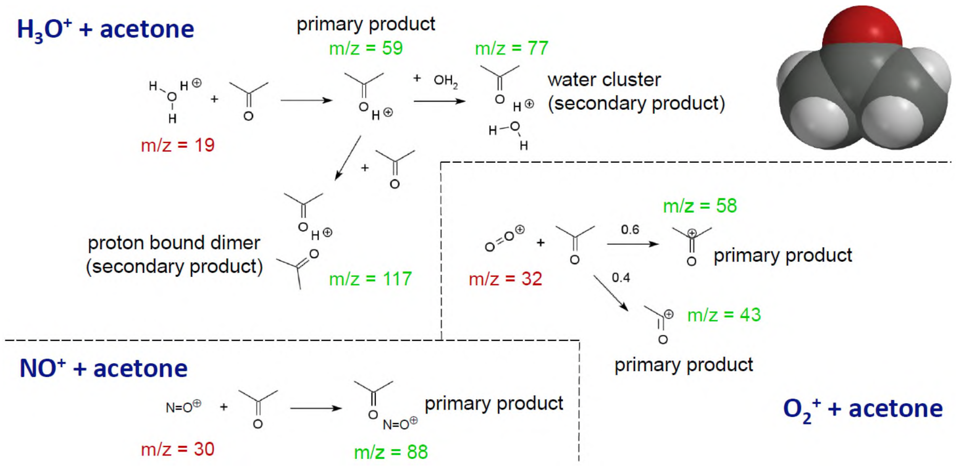


Figure 5: Acetone reactions showing the chemical mechanism. [40]

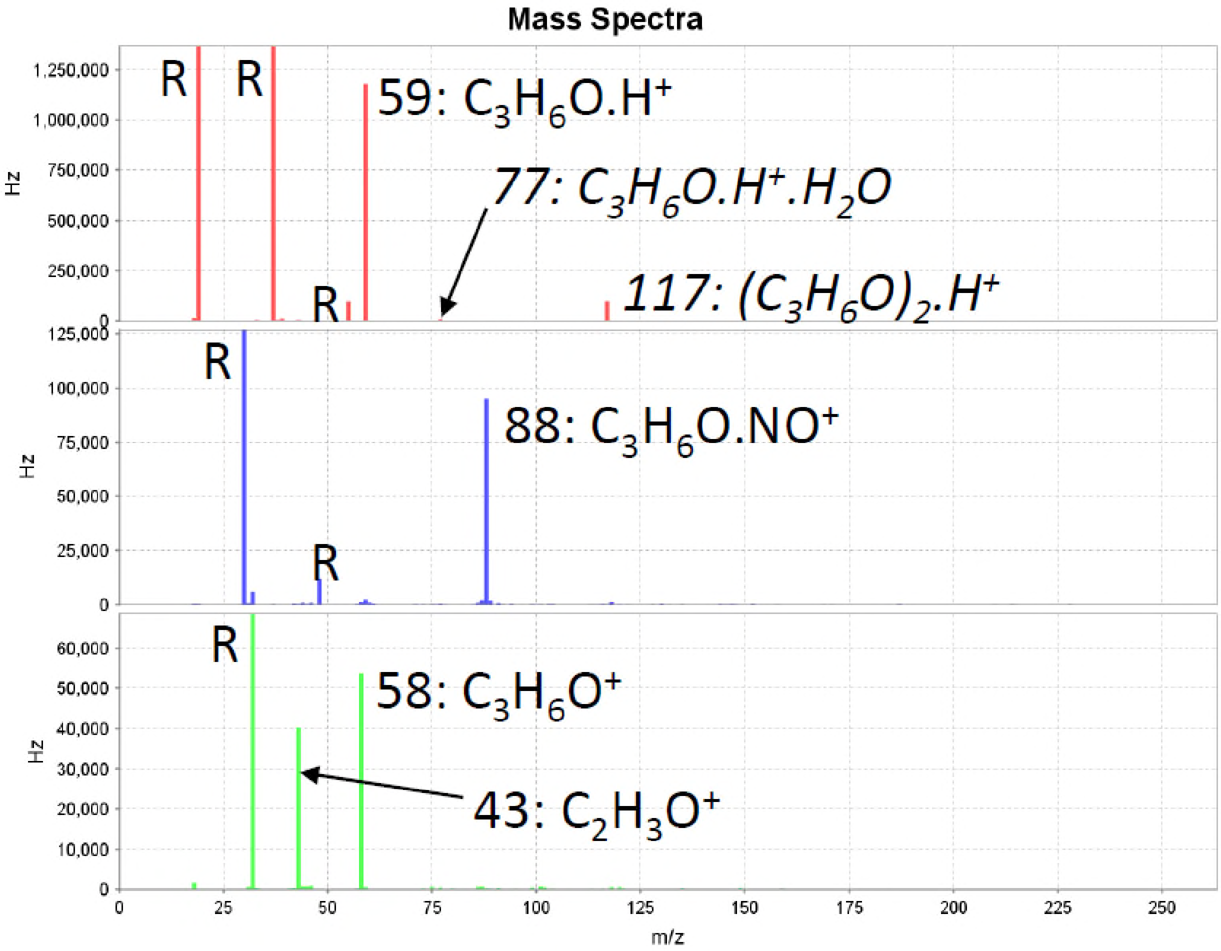


Figure 6: Mass spectra of the different acetone reaction channels. Red: H_3O^+ spectrum, Blue: NO^+ mass spectrum, Green: O_2^+ spectrum. R=Reagent ion peak. [40]

2.2.3 Kinetics and Quantification of SIFT-MS

The following derivations and formulae are adapted from a collection of publications and internal SIFT-MS training material, provided by the company Syft Technologies and by Syft Technologies' Founding Professor, Murray McEwan. [37, 41, 42]. In the following chapter only an overview of the background of the kinetics and thus the quantification of the SIFT-MS technique is given. The research of Ferguson et al. [22], Bolden et al. [43] and Adams and Smith [44] provide further information regarding the Flowing Afterglow and SIFT techniques, which are theoretically very similar. Additionally, the research of Spanel and Smith [33, 45, 46] and Freeman and McEwan [47] provide further information regarding the SIFT-MS analytical methodology.

We start with a typical SIFT-MS ion molecule reaction, where $R+$ is the reagent ion, A the analyte and P^+ the product ion:

$$R^+ + A \rightarrow P^+$$

For an ion-molecule reaction, the rate equation expressing the decrease in concentration of A with time t of the reaction is:

$$-\frac{d[R^+]}{dt} = k[R^+] \bullet [A] \qquad (1.0)$$

where k is the rate constant for the reaction between R^+ and A and t the reaction time of R^+ and A in the SIFT-MS flow tube. This time is determined by the flow velocity of ions in the flow tube.

To solve the rate equation for SIFT-MS flow tube conditions, it has to be known that the concentration of the analyte $[A]$ is always very much larger than the reagent ion concentration $[R^+]$.

$$[A] >> [R^+]$$

Therefore, $[A]$ is treated as a constant in the rate equation, which simultaneously results in application of a pseudo-first order rate law. As the reaction time t is defined as the reaction length l divided by the velocity of the ions sampled in the flow gas (v_0 in cm • s^{-1}), equation 1.0 can be integrated to become equation 1.1, where $[R_0^+]$ is the initial concentration of R^+. In this equation z displays the distance in the flow tube.

$$[R^+] = [R_0{}^+] \bullet exp\left\{-\frac{k}{v_0} \bullet \int_0^l [A]dz\right\} \qquad (1.1)$$

Imposing pseudo-first order kinetics, it is assumed that:

1. The analyte A is evenly distributed radially through the entire length of the reaction region in the flow tube (Analyte is mixes efficiently with the carrier gas) and
2. That $\varphi_{analyte}$ is the flow of analyte A in molecules • s$^{-1.}$

A can then be approximated to following equations 1.2 and 1.3, where a is the radius of the flow tube and z is some distance of the entire reaction length l.

$$[A] = 0 \; if \; z < 0 \qquad (1.2)$$

$$[A] = \frac{\varphi_{analyte}}{\pi \bullet a^2 \bullet v_0} \; if \; z \geq 0 \qquad (1.3)$$

Equation 1.1 can now be evaluated to determine the rate law for a bimolecular reaction where the pseudo-first order approximation is applied.

$$[R^+] = [R^+]_0 \bullet exp\left\{-\frac{k \bullet \varphi_{analyte} \bullet l}{\pi \bullet a^2 \bullet v_0{}^2}\right\} \qquad (1.4)$$

The intensities of R^+ and R_0^+ in counts per second (cps) are directly proportional to the ion concentrations in the flow tube:

$$\ln\left\{\frac{I(R^+)}{I(R_0{}^+)}\right\} = -\frac{k \bullet \varphi_{analyte} \bullet l'}{\pi \bullet a^2 \bullet v_0{}^2} \qquad (1.5)$$

Where,

- k is the rate constant for the reaction between R^+ and A
- l' is the reaction length slightly modified to allow for mixing of analytes in the flow tube

As one of the main features of the SIFT-MS technique is its ability to simultaneously measure the concentrations of many analytes in a single sample without prior separation [37], it is apparent that equation 1.5 is insufficient to quantitatively determine multiple analytes simultaneously. For example, a mixture of two analytes introduced to the system, where H_3O^+ is the chosen reagent ion, each analyte would reduce the ion intensity of H_3O^+ and only the total analyte concentration could be found. To quantitate individual analyte concentration, the intensities of the product ions are required to be measured as well as the intensity of the reagent ion. By introducing two separate masses into a single equation, the differential diffusion of the product and precursor ions must now be included under the assumption that the mass discrimination of the downstream quadrupole chamber is known, and inclusion of this term requires equation (1.5) be approached from a different perspective.

Smith and Spanel have worked this out [33] and similar expressions to equation (1.5) have been found for both reagent ions R^+ and product ions P^+, from which the analyte concentration [A] can be found. The analytical solution to the simultaneous equations for both ions is shown below, with *De* expresses a factor that allows for the different diffusion coefficients of the product and reagent ions.

$$[A] = \frac{1}{k \bullet t_r \bullet De} \bullet \frac{P^+}{R^+} \tag{1.6}$$

In equation (1.6):

- R^+ is the reagent ion count rate (in cps)
- P^+ is the product ion count rate (in cps)
- K is the rate coefficient (in $\mathrm{cm}^3 \bullet \mathrm{molecule}^{-1} \bullet \mathrm{s}^{-1}$)
- [A] is the number density of the analyte (in $\mathrm{molecule} \bullet \mathrm{cm}^{-3}$)
- t_r is the reaction time (in seconds)

In Syft Technologies instruments, the *De* factor is incorporated into the Instrument Calibration function (ICF)[2].

---

[2] The ICF is updated daily by analysis of a quantitative gas standard, which contains seven analytes with molecular masses covering the instrument's mass range. By comparing the measured concentrations with the supplier's certified concentrations, multiplication factors to correct the instrument's response are obtained. This allows Syft Voice series instruments to determine absolute concentrations for any analyte found in the Syft compound library. Associated with this, the transferability of compound characterization data from instrument to instrument is also ensured. [37] The ICF corrects the ion transmission. That has to be done because Ions of different mass-to-charge ratios do not traverse the flow tube and detection region with consistent efficiency. To account for this, a transmission function must be determined for each instrument as the flow tube is a function of ion size and shape, but approximates, as a function of mass and detection in mass spectrometry is a function of mass. In addition, determination of the reaction time is part of the daily update. [42]

Replacing De with the *ICF* for the reagent ion R^+ and the product ion P^+ (dimensionless) yields the following equation:

$$[A] = \frac{1}{k * t_r} \bullet \frac{P^+}{R^+} \bullet \frac{ICF_{Prod}}{ICF_{Reag}} \tag{1.7}$$

In terms of the Syft technologies SIFT-MS schematic (see Chapter 2.2.2) the instrument calibration factor γ is:

$$\gamma = \frac{1}{t_r} \bullet \frac{ICF_{Prod}}{ICF_{Reag}} \tag{1.8}$$

Equation (1.7) applies for the simple case when there is no significant secondary chemistry of the reagent ion R^+ and only a single product ion P^+ is formed. General equation accounting for secondary chemistry is:

$$[A] = \frac{{P_i}^+ \bullet ICF_{Prod}(i) + \sum_{all\,ki} {P_{ki}}^+ \bullet ICF_{Prod}(ki)}{t_r \bullet BR_i \bullet \sum_{all\,j} k_j \bullet {R_j}^+ \bullet ICF_{Reag}(j)} \tag{1.9}$$

In equation (1.9):

- R_j^+ is the reagent ion signal (in cps) for the injected reagent ion (j= 0) and its water cluster ions (if appropriate; $j = 1, 2, 3$)
- k_j is the rate coefficient for reaction of reagent ion R_j^+ with the analyte ($cm^3 \bullet molecule^{-1} \bullet s^{-1}$)
- $ICF_{Reag}(j)$ is the transmission factor for the reagent ion R_j^+(dimensionless)
- P_i is the primary product ion signal (in cps) for primary product ion *i*
- P_{ki} is the secondary product ion signal (in cps) for secondary product ion *k* derived from primary product ion *i*
- $ICF_{Prod}(i)$ is the transmission factor for the primary product ion P_i^+ (dimensionless)
- $ICF_{Prod}(ki)$ is the transmission factor for the secondary product ion P_{ki}^+ (dimensionless)
- BR_i is the branching ratio for primary product ion *i* ($0 < i \leq 1$)

The instrument software individually calculates the concentrations for the method selected primary product ions and cross compares them to enhance selectivity. Effectively, with equation (1.9), several $[A]_i$ are calculated for each individual primary product ion channel. Converting from $[A]$ in molecules • cm^{-3} to the concentration in the original gas sample is made from the partial pressure of the analyte in the sample (by using the Ideal gas law) as follows:

$$P_{analyte} = 10^6 \bullet [A] \bullet R \bullet \frac{T_{flow\,tube}}{N_A} \tag{1.10}$$

In this equation:

- $T_{flow\,tube}$ is the temperature in the flow tube (in Kelvin).
- R is the gas constant (62.48 Torr • K^{-1} • mol^{-1})
- N_A is Avogadro's number ($6.022 \bullet 10^{23}$, the number of molecules in a mole)
- $[A]$ is the number density of the analyte, A (molecules • cm^{-3})

Converting $P_{analyte}$ to Torr (mm Hg), which is the chosen pressure unit in Syft Technologies instruments and substituting the constants:

$$P_{analyte}(Torr) = 1.035 \bullet 10^{-19} \bullet [A] \bullet T_{flow\ tube}(K) \tag{1.11}$$

The flow of analyte $\varphi_{analyte}$ is found from the total flow of the gas in the flow tube, which is the sum of the carrier gas flow, φ_{carr} , plus the sample gas flow, φ_{samp} (all in units of Torr • L • s^{-1}). Here, $P_{flow\ tube}$ is the total pressure in the flow tube in Torr:

$$\varphi_{analyte} = \left(\varphi_{carr} + \varphi_{samp}\right) \bullet \frac{P_{analyte}}{P_{flow\ tube}} \tag{1.12}$$

The volume mixing ratio is found by a ratio of the analyte flow to the capillary flow, and then multiplying by the required factor, which is 10^6 for ppmv, 10^9 for ppbv and 10^{12} for pptv. The example for ppbv is given as the following equation.

$$ppbv_{Analyte} = \frac{\varphi_{Analyte}}{\varphi_{Analyte}} 10^9 \tag{1.13}$$

The general expression for determining volume mixing ratio in a sample is then found by combining equations (1.11) and (1.12) and (1.13).

$$[A](ppbv) = 1.035 \bullet 10^{-10} \bullet [A] \bullet \frac{T_{flow\ tube}}{P_{flow\ tube}} \bullet \left(\frac{\varphi_{carr}}{\varphi_{samp}} + 1\right) \tag{1.14}$$

Combining the equation for determining the analyte number density in the flow tube $[A]_i$ for each measured primary product ion i with the sample dilution in the flow tube (1.9), the **master equation** is obtained and $[A]_I$, the volume mixing ratio, in the original sample, can directly be obtained:

$$[A](ppbv) = 1.035 \bullet 10^{-10} \bullet \frac{T_{flow\ tube}}{P_{flow\ tube}} \bullet \left(\frac{\varphi_{carr}}{\varphi_{samp}} + 1\right) \bullet \frac{{P_i}^{+} \bullet ICF_{Prod}(i) + \sum_{all\ ki} {P_{ki}}^{+} \bullet ICF_{Prod}(ki)}{t_r \bullet BR_i \bullet \sum_{all\ j} k_j \bullet {R_j}^{+} \bullet ICF_{Reag}(j)} \tag{1.15}$$

To convert ppbv to a mass-dependent concentration unit as used in this work (µg • m^{-3}), the molecular weight M in g • mol^{-1} of the analyte and the molar volume V_m in m^3 • mol^{-1} must be introduced into the formula. V_m is temperature-dependent; if a temperature of 25 °C is assumed, V_m is 22.45 L • mol^{-1} and the following relationship results:

$$[A](\mu g \bullet m^{-3}) = \frac{[A](ppbv) \bullet M}{V_m} = \frac{[A](ppbv) \bullet M}{0.02245\ m^3 \bullet mol^{-1}} \tag{1.16}$$

2.2.4 Gas-Phase Ionic reactions

The kinetics of chemical reactions in the gas phase are well understood and form the basis of SIFT-MS measurement technology. [37,39]

The reaction rate coefficient of the respective reaction acts as a key parameter that allows quantification. The kinetics of a reaction is crucial for the successful application of the SIFT-MS technique, but the thermodynamics of a reaction must not be ignored. This is because a thermodynamically unfavorable process will most likely not take place in the gas phase.

If potential energy surfaces do not have an activation energy barrier, reactions in the gas phase are often so fast that each collision results in production. This is the case with ion-neutral reactions. The reaction rate coefficient is then equal to the coefficient of collision limiting rate. Each reagent ion reacts in a different way due to thermodynamic constraints. The reaction pathways observed in the SIFT-MS technique are explained below. However, before going into the individual reaction mechanisms in more detail, Table 3 shows an overview of the mechanism of the individual reagent ions.

Table 3: Reaction pathways of SIFT-MS reagent ions.

Mechanism	H_3O^+	NO^+	O_2^+	OH^-	O^-	O_2^-	NO_2^-	NO_3^-
Proton transfer (PT)	✓	×	×					
Electron transfer (ET)	×	✓	✓	×	×	✓	×	×
Dissociative ET	×	✓	✓					
Hydride abstraction	×	✓	×					
Association	✓	✓	×	✓	✓	✓	×	×
Proton abstraction				✓	✓	✓	✓	✓
Hydrogen atom transfer				×	✓	×	×	×
Associative detachment				✓	✓	✓	×	×
Displacement				✓	✓	×	×	×
Elimination				✓	✓	×	×	×

2.2.4.1 Proton transfer

Proton transfer is one of the most famous reaction mechanisms of soft chemical ionization used in mass spectrometry. A protonated reagent ion (H_3O^+) reacts with the target molecule to form an ionized form of the molecule. For the reaction to take place, the proton affinity of the analyte molecule must be greater than that of the non-protonated form of the reagent ion. For reactions with H_3O^+, the proton affinity of the analyte molecule must therefore be greater than the proton affinity of water (691 kJ • mol^{-1}) for a reaction to take place. If so, the efficiency of the proton transfer is 100 %, which means every collision yields to a protonated product ion of the molecule. An example of a proton transfer reaction is given below, where H_3O^+ transfers a proton to acetone. [28]

$$H_3O^+ + (CH_3)_2CO \rightarrow (CH_3)_2COH^+ + H_2O + 121\ \text{kJ} \cdot \text{mol}^{-1}$$

2.2.4.2 Electron transfer

Electron transfer reactions are quite closely related to what is observed as electron impact ionization, used for example in GC-MS instruments. Due to the hardness of ionization in typical electron impact spectrometers, this particular mechanism is not significant for most compounds. Since in SIFT-MS spectrometers the ionization is much softer, the mechanism of electron transfer is much more significant. The mechanism is also known as charge transfer.

The general mechanism is:

$$\text{Ion A} + \text{Molecule B} \rightarrow \text{Ion B} + \text{Molecule A}$$

For positively charged reagent ions, the electron is taken from Molecule B, and therefore the ionization energy must be lower than that of the neutral form of the reagent ion (Ion A). If the reagent ion is negatively charged, the electron is given to molecule B and therefore, the electron affinity of molecule B must be higher than that of the neutral form of the reagent ion (Ion A). That means a more stable negatively charged product is formed than Ion A.

The SIFT-MS reagent ions O_2^+ and NO^+ will undergo the process of electron transfer when the ionization energy of the analyte molecule is less than 12.07 eV and 9.26 eV, respectively. An example of cationic electron transfer between $O_2^{\bullet+}$ and benzene is given below, where benzene donates an electron to $O_2^{\bullet+}$. [48]

$$O_2^{\bullet+} + C_6H_6 \rightarrow C_6H_6^+ + O_2 + 2.8\ \text{eV}$$

For anionic electron transfer there is an example of the reaction of O_2^- with nitrogen dioxide given below. [49]

$$O_2^- + NO_2 \rightarrow NO_2^- + O_2$$

Electron transfer processes are often dissociative. In this case, the molecular ion, which has been formed as a result of the electron transfer, breaks into smaller fragments. The excess energy of the electron transfer process causes bond breaking in the product ion. An example of a dissociative electron transfer reaction is given as the following reaction of the reaction of $O_2^{\bullet+}$ with n-butane. [29]

$$O_2^{\bullet+} + n\text{-}C_4H_{10} \rightarrow C_3H_7^+ + O_2 + CH_3 + 0.9\ \text{eV}$$

As already described, O_2^+ and NO^+ can both react via the electron transfer and dissociative electron transfer mechanisms. Due to the higher ionization energy of O_2^+ compared to NO^+, O_2^+ reacts with more compounds than NO^+. The higher ionization energy of O_2^+ also means that dissociative electron transfer is more likely for O_2^+.

2.2.4.3 Hydride abstraction

The hydride abstraction mechanism is most commonly observed for NO^+. Abstraction of hydride (H^-) in a SIFT-MS flow tube leads to an $[M - H]^+$ cation. An example of the abstraction of hydride by NO^+ from acetaldehyde is shown as following reaction. [28]

$$NO^+ + CH_3CHO \rightarrow CH_3CO^+ + NOH + 52.9\ kJ \bullet mol^{-1}$$

The reaction is determined by the parameter hydride affinity. Where the hydride affinity of the reagent ion is greater than that of the conjugate base of the analyte, the reaction will proceed as an exothermic pathway. The hydride abstraction mechanism will often occur with 100% collision efficiency, but is also known to occur very slowly with a collision efficiency of less than 10^{-3}. [50]

The types of compounds which this mechanism is favored for are those that have a hydrogen where the hydride loss can be stabilized easily, e.g., branched alkanes and also aldehydes and alcohols. This provides the ability to SIFT-MS to distinguish between branched and straight chain alkanes, especially at low molecular weight. [49]

2.2.4.4 Association

There are two different pathways by which association can occur: radiative [51] and termolecular [52] association. Examples for both are given below:

$$\text{Radiative:} \quad NO^+ + c\text{-}C_6H_5CN \rightarrow NO{\bullet}C_6H_5CN^+ + h\nu$$

$$\text{Termolecular:} \quad NO^+ + CH_3OH + He \rightarrow NO{\bullet}CH_3OH^+ + He$$

It is assumed that radiation association paths do not occur in SIFT-MS, because the radiation lifetime of a collision complex is much longer than the mean free path length of an ion in the flow tube (~50 µm). Bates and Herbst [53] define the upper pressure limit at which radiation association occurs as 10^{12} molecules • cm^{-3}, meaning four orders of magnitude lower than the pressure range of a SIFT-MS flow tube. Thus, the ion does not have enough time to emit a photon before it collides with many different carrier gas atoms. It is therefore assumed that, in the case of SIFT-MS technology, all association processes take place via the process of termolecular association.

Termolecular association is a three-body collision of the reagent ion, the analyte and a non-reactive species. The reagent ion attaches itself to the analyte and the “third body” M carries away excess vibrational and rotational energy that would otherwise cause the reagent ion and the analyte to separate. [53] The third body allows for stabilization of the collision complex at an energy less than the energy required to dissociate the complex. The energy that is removed by the third body is known as the binding energy. [54, 55] The “third body (collision partner)” can be a carrier gas atom, or nitrogen or oxygen from the air sample. Sometimes these reactions are very inefficient. But efficiency is increased by pressure, because this increases the probability of three-body collisions. [37]

The mechanism of association occurs with both positive and negative reagent ions. The mechanism occurs frequently for ketones, organic acids and unsaturated hydrocarbons, and is most commonly observed for NO^+ and occur occasionally for H_3O^+ and their respective water clusters. In general association reaction are more common with negatively charged reagent ions. [37, 49]. In the following examples for the mechanism of association are given [37].

1. NO^+ + Acetone $NO^+ C_3H_6O + M \rightarrow C_3H_6O{\bullet}NO^+ + M$
2. OH^- + Water $OH^- + H_2O + M \rightarrow OH^-{\bullet}H_2O + M$
3. O_2^- + Carbon dioxide $O_2^- + CO_2 + M \rightarrow O_2^-{\bullet}CO_2 + M$

The following mechanisms only occur with negative reagent ions. These are the mechanisms of proton abstraction, hydrogen atom transfer, displacement, elimination and associative detachment.

2.2.4.5 Proton abstraction

Proton abstraction is the opposite of proton transfer with H_3O^+. A proton, i.e., H^+ is transferred from the analyte molecule to the reagent ion. An example is given for the reaction of OH^- with methanol. [37]

$$OH^- + CH_3OH \rightarrow CH_3O^- + H_2O$$

The mechanism occurs for exothermic reactions.

2.2.4.6 Hydrogen atom transfer

In hydrogen atom transfer reactions, a hydrogen atom is transferred from the analyte molecule to the reagent ion. These reactions occur for the reagent ion O^- and are common with low molecular weight hydrocarbons. An example is the reaction of O^- with hexane [37].

$$O^- + C_6H_{14} \rightarrow OH^- + \text{Product(s)}$$

2.2.4.7 Displacement

Displacement frequently occurs as one of several mechanisms observed for reactions of OH^- with small, halogenated organics. The generalized mechanism for displacement is:

$$A^- + RB \rightarrow RA + B^-$$

A stands for the reagent ion and B for a halogen. A concrete example is the reaction of OH^- with methyl chloride:

$$OH^- + CH_3Cl \rightarrow CH_3OH + Cl^-$$

Detection takes place at m/z of the displaced ion (-35 and -37 for reactions with chlorides).

2.2.4.8 Elimination

Elimination is also a reaction occurring with halogenated compounds. In contrast to the mechanism of displacement, for the reaction mechanism of elimination to occur the halogenated analyte has to contain at least three carbon atoms. The general mechanism, where R’ is an alkene and R” is a substituted alkane, is displayed below [37]:

$$A^- + RB \rightarrow R' + R''A + B^-$$

Similarly with displacement reactions, detection takes place at m/z of the displaced ion.

2.2.4.9 Associative detachment

The associative detachment reaction mechanism yields the most noticeable difference between negative and positive ions. When A is the molecule of interest and R the reagent ion, this general mechanism describes associative detachment:

$$R^- + A \rightarrow RA + e$$

Associative detachment can be a major channel for some reactions. Examples:

$$O^- + C_2H_2 \rightarrow C_2H_2O + e \qquad BR = 0.60$$

$$\rightarrow C_2^- + H_2O \qquad BR = 0.05$$

$$\rightarrow C_2H^- + OH \qquad BR = 0.30$$

$$\rightarrow C_2HO^- + H \qquad BR = 0.05$$

The mechanism of associative detachment occurs in SIFT-MS but is actually more a problem than a help with analyzing compounds. The reason is that this mechanism basically results in reagent ion loss. [49]

3 Materials and methods

This chapter describes the equipment and methods used for test gas generation. The functionality of the dynamic test gas facility used in the IFA is explained. In addition, various dosing systems that are used for test gas generation at the IFA and during this work are described.

3.1 Generation of test gases at a dynamic test gas facility at the IFA

As mentioned previously, IFA uses a dynamic method for its test gas generation during proficiency tests. In addition to proficiency testing, the generated test gas is also used for calibration and validation of analytical equipment and for method development. In Figure 7 a schematic diagram of the dynamic test gas facility is displayed. Setup, operating principle and different sections will be described in the following.

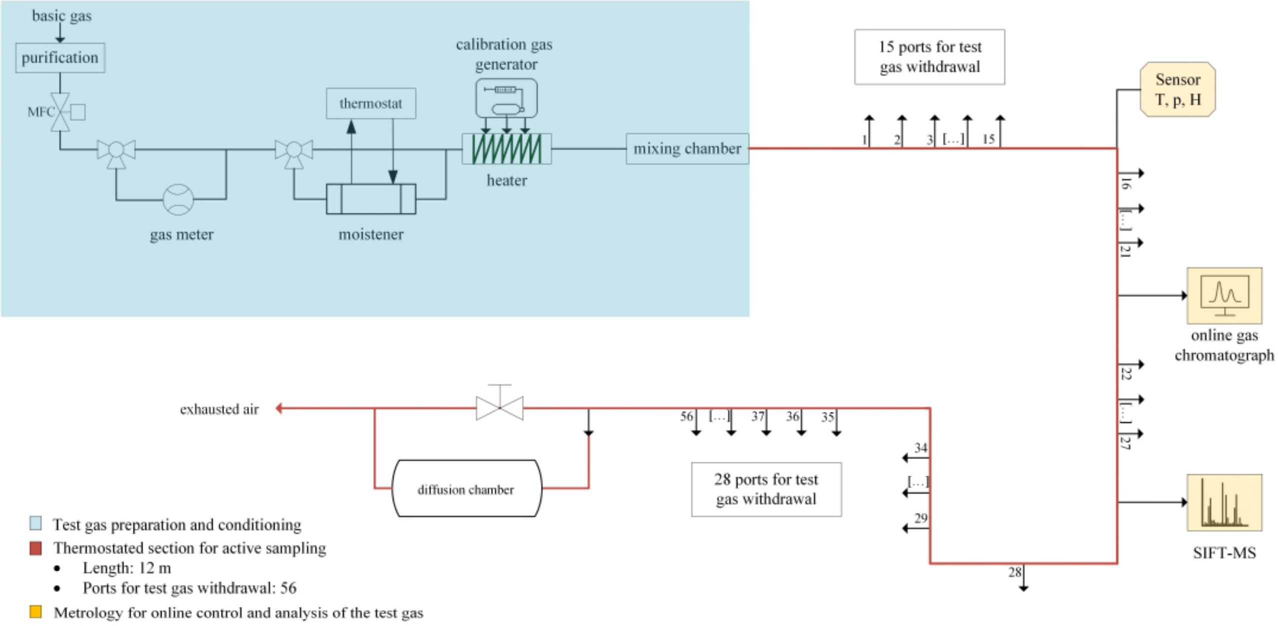


Figure 7: Schematic diagram of IFA´s dynamic test gas facility.

The entire test gas facility is 15 meters long and is made up of a glass tube with an inner diameter of 50 mm. Within flow-rates from 1-6 m³ per hour a laminar flow with homogenous test gas along the whole tube has been demonstrated [10, 15]. In the first part of the facility, test gas preparation and conditioning takes place. That includes basic gas supply, humidifier unit, different types of dosage systems and a mixing chamber. After conditioning, the tempered section for withdrawal follows, where a homogeneous test gas is provided over a distance of 12 m. Test gas can be extracted at 56 sampling ports, equipped with Y-distributors. Different systems for online control are distributed over the whole section for sampling. For one thing, environmental conditions as temperature, pressure and relative humidity are recorded and for another thing, the applied online analytical techniques fast-GC-FID and SIFT-MS are constantly obtaining data on the quantitative composition of the test gas.

3.1.1 Control section of the dynamic test gas facility

For generation of the dynamic test gas, vaporized analytes are continuously added to a basic gas flow. The basic gas (compressed air, dried and pre-cleaned) is additionally purified in a combustion air treatment plant. The basic gas with gaseous hydrocarbon residues is passed through a heated platinum catalyst (450°C) and finally purified through two adsorption units filled with (active carbon and purafil). The purified basic gas stream is passed to the facility, controlled by a mass flow controller (Analyt MTC Series-M) and additionally monitored by a gas meter. The flow rate is adjustable from 1 – 6 m^3/h, depending on the experiment. The set flow rate is based on the sampling procedure and is chosen such that the provision of a homogeneous test gas is guaranteed over the entire sampling section. The primary test gas flow must in any case be approximately 20 % higher than all volume flows taken together from the test gas line during a test. The 20 % surplus is a value based on experience gained during many years of operation of the test gas facility. As mentioned before, the relative humidity in the facility is adjustable from 10 – 80 % to simulate different conditions during sampling in workplace environments. Furthermore, the temperature can also be varied between 10 °C and 40°C.

To achieve different humidity levels, the basic gas stream is divided by a control valve and proportionately conducts the water surface of the humidifier unit. To set high humidity levels the water can additionally be heated by a circulation thermostat to increase the evaporation of water. After merging the two gas streams, analytes are continuously added to the humidified basic gas. This takes place in different ways depending on the added substance groups and their properties respective to the target concentration. For the investigated substances and proficiency testing schemes in this thesis, different dosage devices are in use. A detailed description of the operating modes is given in Chapter 3.2.

3.1.2 Inlet zone of the dynamic test gas facility

Condensation effects are prevented at the injection point of the test gas facility by heating the glass tube from outside. The temperature is set in accordance with the component with the highest boiling point and is set 10 °C higher due to the temperature gradient through the glass wall in order to reach the target temperature inside. Two heating bands work according to the setpoint/actual value principle, whereby the upper limit of the control range is set to the set temperature plus 10 °C. To homogenize the test gas, the heated inlet point is followed by a mixing chamber (length 80 cm), filled with a pile of short glass tubes of about 1 cm length and 5 mm inner diameter and a settling section of 50 cm in front of the section for active sampling.

3.1.3 Section for active sampling

To ensure reproducible and constant ambient conditions over the entire section for active sampling, the whole test gas facility is thermally insulated and connected to three temperature control baths. For one thing, that leads to constant ambient conditions inside the glass tube and for another thing, it enables testing methods on temperature effects in a method development process.

3.1.4 Equilibration of test gases

An equilibration period of at least 30 minutes must be observed before the concentrations are set to their targets. Depending on the substances, a longer equilibration time may be required. This is mainly justified by different polarity of the substances. Similar to chromatography, the adsorption of polar substances onto the internal glass walls of the apparatus is more pronounced than that of non-polar compounds. This behavior can be observed with polar glycol ethers and esters, for example.

3.2 Dosing systems for generating test gases at the IFA

3.2.1 Injection dosing pump

For the proficiency testing schemes involving VOCs (concentration range $\mu g/m^3$) and organic solvents (concentration range mg/m^3), an injection-dosing pump is used. This pump operates on the push-pull principle using two gas-tight precision syringes, thus ensuring an accurate and continuous dosing rate. IFA uses the calibration test gas generator HovaCAL® digital 321-SP with HovaPOR® evaporator.

Figure 8: HovaCAL® digital 321-SP and HovaPOR® evaporator. [56]

A picture and the operation of the calibration gas generator is shown in Figure 8 and Figure 9. After the mixture of analytes has been weighed in the requested mass fraction, the mixture is dosed with the syringe pumps into an evaporator, where the analyte vapor is mixed with a mass flow-controlled carrier gas flow at a previously set evaporation temperature of maximum 200 °C. The evaporation temperature is based upon the component with the highest boiling point and is usually set ten degrees above that value to ensure complete continuous evaporation of all components. The

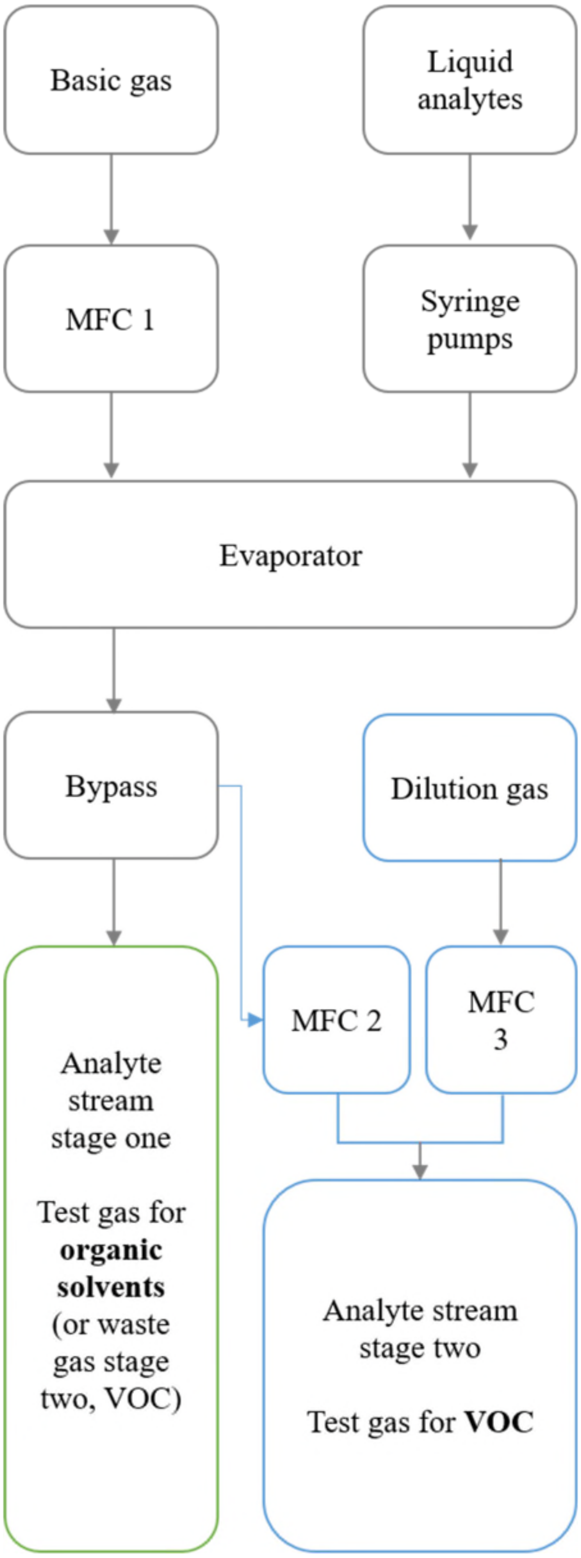


Figure 9: Schematic diagram of the HovaCal® digital VOC 321-SP calibration gas generator. In green: Stage 1 for generating test gases in the mg/m^3 range. In blue: Stage 2 for generating test gases in the $\mu g/m^3$ range. [57]

evaporated analyte gas mixture leaves the evaporator unit and can be added directly to the main flow. This operating mode is used to generate test gas atmospheres in the mg/m³ range for organic solvents. Whereas in the preparation process for VOC test gas in the µg/m³ range, the calibration gas generator operates in a two-stage dilution mode. Therefore, the analyte gas stream of stage one is split and the minor part (0.5 – 10 mL•min^{-1}) of this gas stream is diluted with a mass flow-controlled make-up gas stream (100 – 2000 mL•min^{-1}) before it is added to the main flow. The concentration of stage one can thus be diluted by a ratio of up to 1:4000. [57]

3.2.2 Permeation oven for generation of formaldehyde test gas

Paraformaldehyde is the polymerization product of formaldehyde and the smallest polyoxymethylene. It forms in aqueous formaldehyde solutions as a white precipitate. For formaldehyde, the depolymerization of paraformaldehyde under heating has proven to be a particularly suitable process for the production of test gases. One way to produce a formaldehyde test gas is through dry heating of paraformaldehyde in a diffusion chamber under controlled conditions [58]. Therefore, a permeation oven is used to generate constant amounts of formaldehyde test gas from a permeation tube Figure 10. Before the first use, the tube must be conditioned to achieve stabilized emissions of formaldehyde. The currently used permeation tube was filled with paraformaldehyde in 2015 and has been used in the aldehyde proficiency testing scheme since 2016.

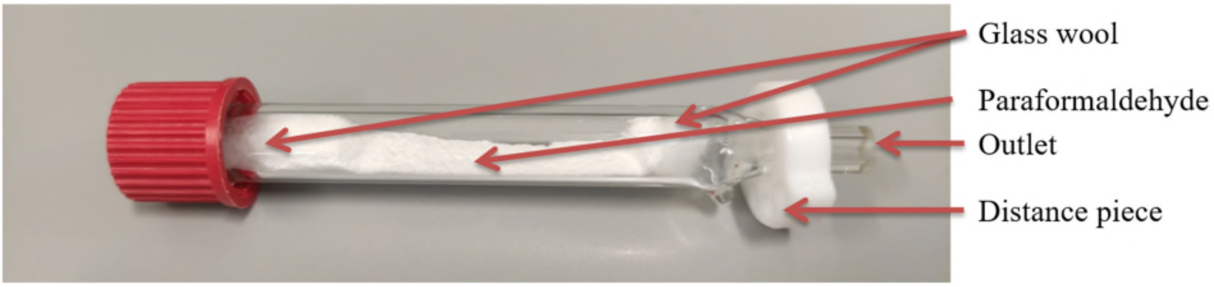


Figure 10: Permeation tube used for formaldehyde test gas generation.

The concentration of formaldehyde is determined indirectly by the temperature of the chamber in the permeation oven. At this point the behavior of the permeation tube used is well known and is still stable in its permeation rate. The concentrations determined so far at different temperatures are collected and, with these data, the formaldehyde concentration can be predicted relatively accurately. A graph showing the performance data of the last few years during proficiency testing is shown in Figure 11. Because formaldehyde is one of the substances in the aldehyde proficiency testing scheme, it gets an external check once a year as well.

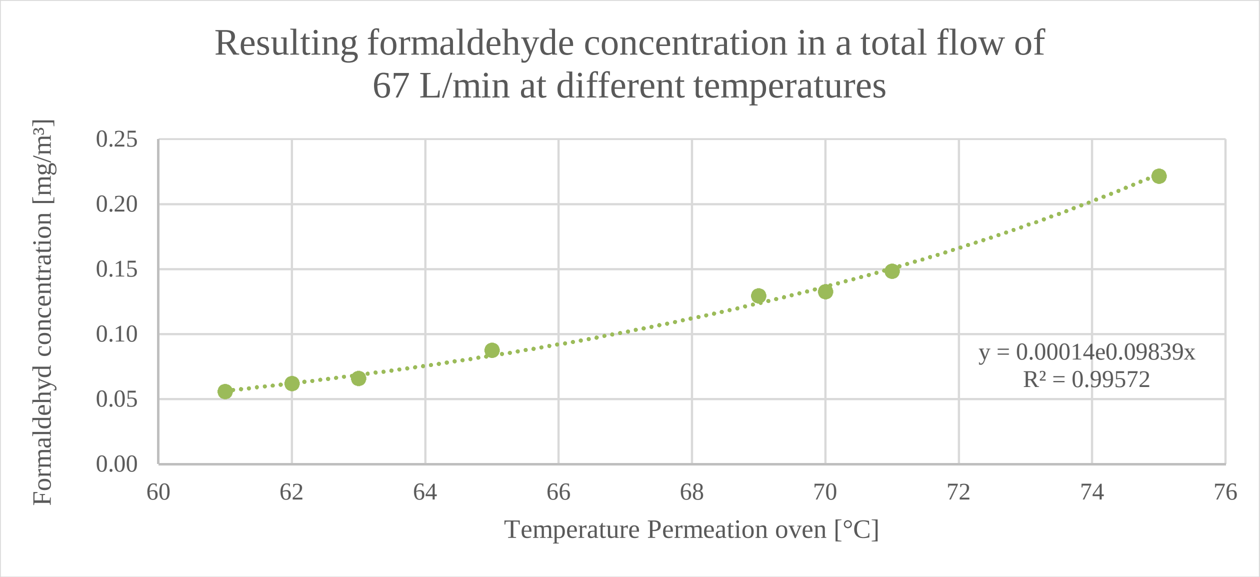


Figure 11: Formaldehyde concentration related to permeation oven temperature.

For practical application, the permeation oven MK 15 from the company Umwelttechnik MCZ GmbH is used. A picture of the device is shown in Figure 12. The oven has five permeation chambers, which can be controlled separately.

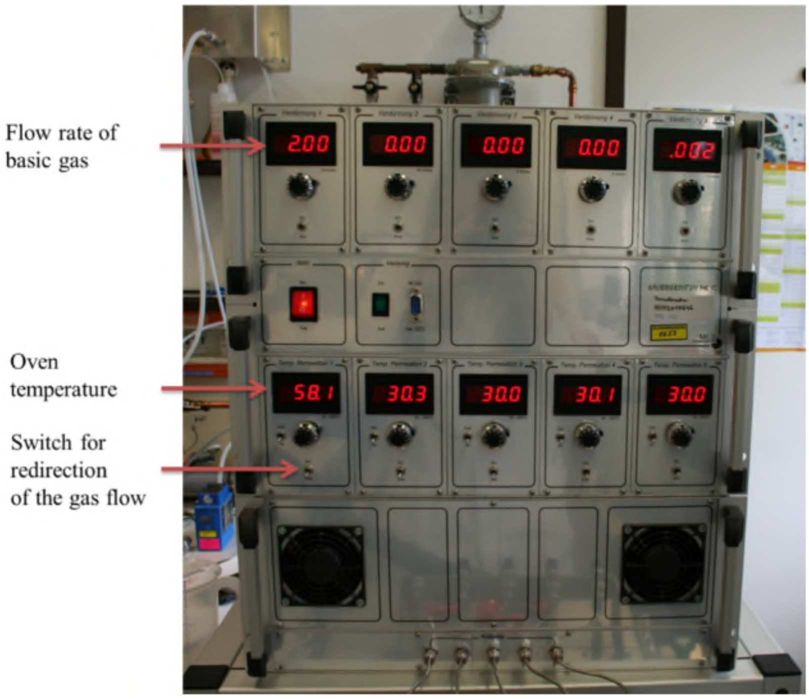


Figure 12: Permeation oven MK 15 from the company

In the upper part of the front panel, the volume flows are set with the aid of dials. In the lower part of the front panel, the temperatures are similarly adjusted. The lower toggle switch is used to divert the gas flow from the respective chamber either to the exhaust gas outlet or to the test gas facility. To minimize the contact area of the permeation tube in the oven, a distance piece is placed at the outlet end. Further information about settings during the experiments is given in Chapter 5.5.1.

3.2.3 Generating test gases from liquid aldehydes as methanolic solution

In addition to formaldehyde (Chapter 3.2.2), acetaldehyde, propionaldehyde and butyraldehyde are other analytes in the proficiency testing scheme for aldehydes. These aldehydes are liquid at room temperature (acetaldehyde Bp: 20.2 °C; propionaldehyde Bp: 49 °C and butyraldehyde Bp: 74.8 °C) and must be dosed differently. Here, a syringe-dosing device: infusion pump Precidor type 5003, Infors AG (Figure 13) is used. The liquid aldehydes are weighed into a methanolic solution and are dosed with a 5 mL syringe. To achieve different concentrations and concentration ratios of the individual aldehydes, several dosing solutions with varying aldehyde concentrations are prepared and all dosed at a constant rate. Due to the high vapor pressure of the aldehydes, the entire dosage system must be cooled. For this purpose, the syringe dosing apparatus is set up in an insulating box, which is provided with hose windings. Ethylene glycol cooled in a thermostat is passed through the hose assemblies. In addition, cooling batteries pre-cooled at -18 °C are placed inside the insulation box. These precautions enable the temperature in the box to be kept permanently below 5 °C throughout the entire dosing period.

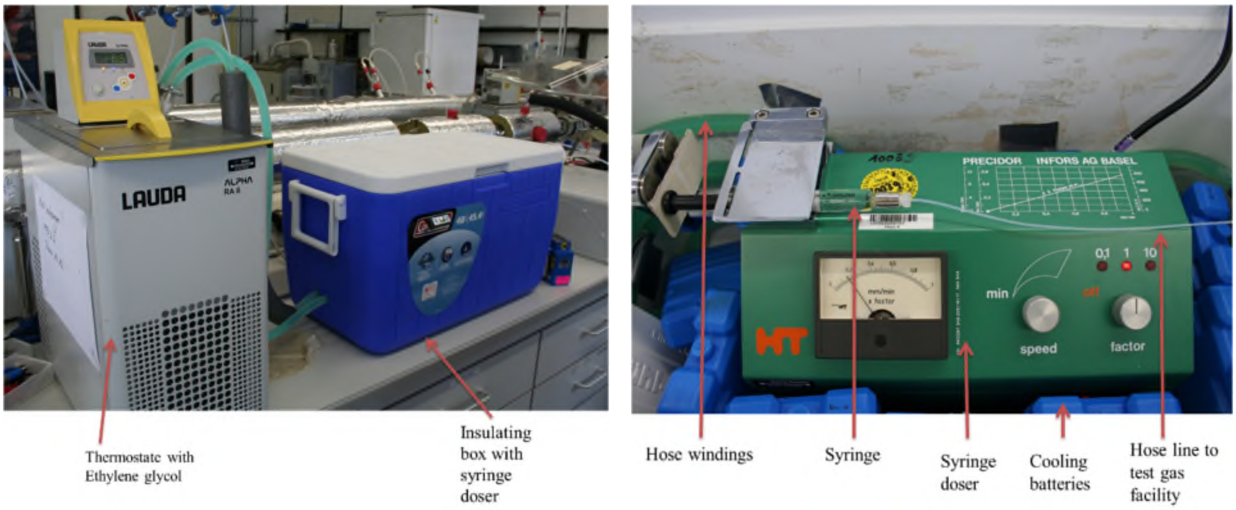


Figure 13: Left: Setup for dosing liquid aldehydes to the test gas facility. Right: Syringe doser inside insulating box.

The aldehydes are vaporized at 90 °C at the point of introduction of the test gas line. Due to the high vapor pressures, this happens there immediately and completely. [17]

Although in the past all proficiency testing schemes could be successfully carried out with this method, especially with regard to technical progress, there is a need to optimize the dosing process. It is noticeable here, in contrast to the other dosing methods, that the aldehydes are not dosed as pure substances but in methanolic solution. Methanol was chosen as solvent because it does not cause any problems during the subsequent offline analysis by HPLC and evaporates quickly due to its high vapor pressure. However, methanol is a hazardous substance, which, if not essential, should be eliminated from the process due to its hazardousness. The second reason for the effort to remove methanol from the process is that large amounts of methanol do not occur in actual workplace air. Since the proficiency testing schemes should be as close as possible to real conditions, methanol-free dosing is desirable. The reason why the aldehydes are dosed as a methanolic solution so far is due to the precision of the syringe feeder used for this application.

3.3 Design of a contactless microfluidic pressure-controlled dosage device

To achieve the desired concentration of 0.1-3 mg/m³ at a given total flow of 67 L/min by dosing pure aldehydes, the dosing rate is between 0.008 and 0.254 µL/min, depending on the Aldehyde. This is a challenge even for modern pump technologies in the commercial sector, especially with regard to the required precision for proficiency testing. The syringe dispenser used to date is obviously not suitable for this task.

In order to establish a new dosing system, first the requirements for the system are defined. Roughly, the system can be divided into three tasks or different parts:

- Precise transfer of the substances;
- Cooling of the aldehyde-contacted device parts to maximum of 5 ºC; and
- Evaporation of the aldehydes.

During the market investigation, it was found that there is no commercially available pump that meets the requirement to deliver the necessary metered quantities in the required precision range and can be cooled at the same time without affecting the electrical parts. The three requirements listed above must therefore be fulfilled from different devices and properly combined.

From this problem, the idea came up to raise the dosing rate in order to guarantee the required precision and in return, to dilute the vaporized substances somehow before they are added into the test gas facility.

3.3.1 Pump selection

Thus, the availability of suitable pumps could be improved enormously. However, it is still problematic that in most pumps the delivery tubing is not separated from the mechanical and electrical parts of the pump as, for example, in a peristaltic pump; moreover, these parts require a higher operating temperature than 5 ºC. Only one pumping system was found, which seems to fulfill both criteria: precise dosing in the lower µL/min range and having electrical components that are separated from aldehyde-contacted devices like the reservoir and the tubing. This is due to the special pump technology and the open construction system of the selected pump from the manufacturer Fluigent. This system is usually used in microfluidics for applications with droplets, cell biology, and particle studies. The pump (Flow EZ™) has a pressure-based flow control system. In the base configuration, the system controls pressure, and the liquid flow is a function of system resistance, fluid viscosity, etc. The addition of a flow meter enables one to control or monitor flow rate as well as dispense desired volumes. The pressure automatically adjusts in the background to maintain the flow rate. The flow is pulse free and has a higher stability (±0.5 %) than a precision syringe pumps (±3.2 %), measured at 5 µL/min (with water). [59] The specified accuracy of the flow unit is 0.21 µL/min at flow rates below 4.2 µL/min for isopropanol.

The chosen flow meter has an inner diameter of 150 µm and the contacted materials of the dosed substance are PEEK and quartz glass. The flow-rate acquisition is based on thermal technology. A heating element on the microchip adds a minimal amount of heat to the medium for the thermal flow measurement. Two temperature sensors symmetrically located before and after the source of the heat detect temperature differences (Figure 14) thus providing the basic information about the spread of the heat, which itself is directly related to the flow rate.

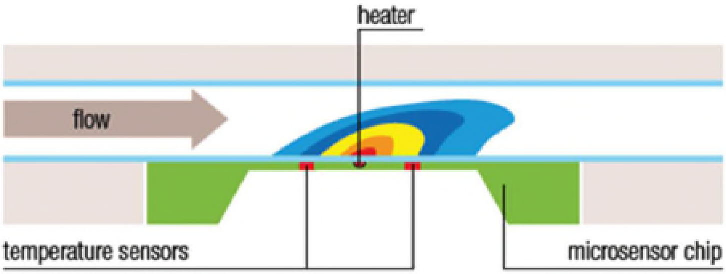


Figure 14: The flow-rate acquisition principle. [60]

All tubing consists of PEEK material. The chosen inner diameter for obtaining the desired flow rate within the pressure limits of the pressure pump (maximum pressure 1000 mbar) is 0.005” (127 µm). To keep the dead volume low, the length of the tubing is kept to a minimum. The pressure required for stable delivery of the desired flow rate is kept as low as possible under atmospheric pressure at the outlet. That is done by keeping the restriction of the tubing relatively low. Further explanations of the interaction between pump and evaporator pressure follow in Chapter 3.3.3.

The flow meter is delivered with two factory calibrations, flow calibration for water and for isopropanol. By means of a conventional syringe pump, the calibration can be adjusted for the medium to be pumped. The setup for calibration of the flow units is displayed in Figure 15 below.

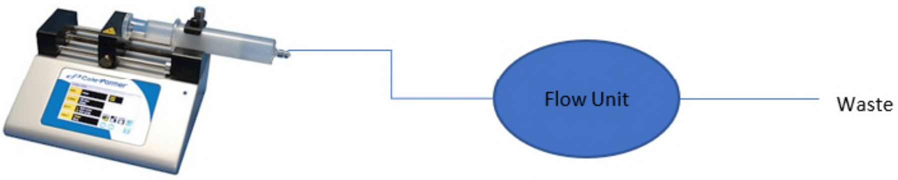


Figure 15: Setup for calibration of the flow units. [61]

The flow rates are set on the syringe pump to the desired rates and the measured flow rate data are recorded with the instrument software. The measured flow rate refers to the measured flow rate on the selected calibration (water or isopropanol). Accordingly, the flow rate set on the syringe pump differs from the measured flow rate. Based on these data, a correction function is created for the corresponding substance. After removing the settling times of the pump, the logged average measured flow rate (X) is plotted vs. set flow rate (Y) of the syringe pump and the best fit up to order 3 is generated and the correction function is stored in the software. Below (Figure 16), the correction functions of the flow units for acetaldehyde, propionaldehyde and butyraldehyde are shown.

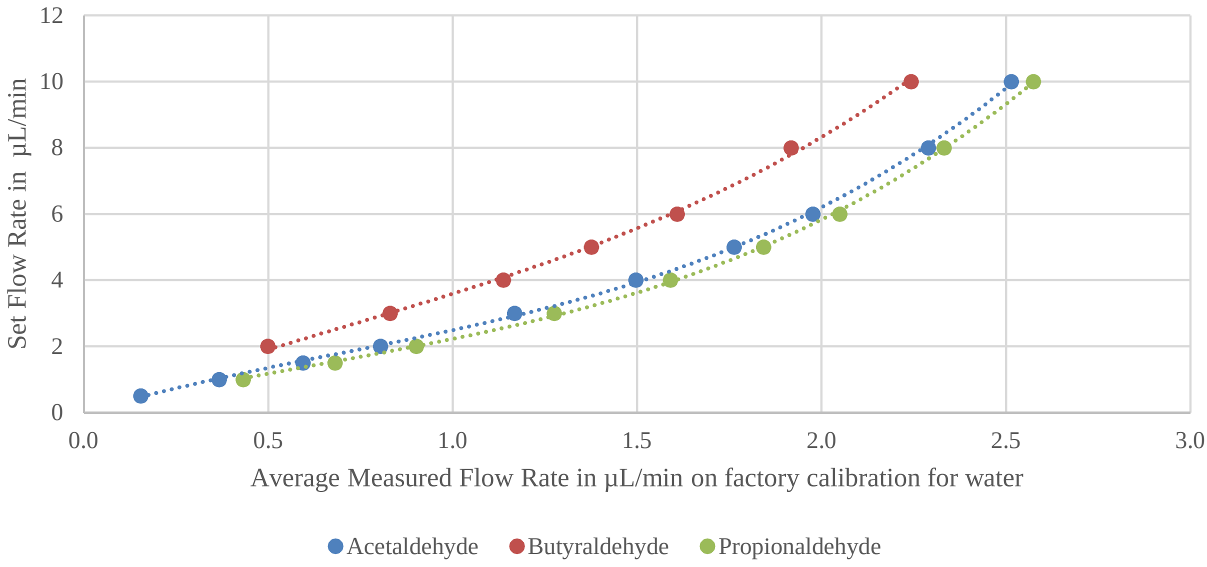


Figure 16: Flow unit calibration for aldehydes.

Butyraldehyde only provides a stable flow rate in the flow unit at 2 µL/min. Therefore, 2 µL/min is the lowest flow rate that can be selected if the concentration setting is to be achieved with the same dosing rate for each aldehyde and varying split ratios (see chapter 3.3.3). The determined correction functions (for nonlinear calibration) are shown in the following:

Acetaldehyde $y = 0.6823x^3 - 1.4368x^2 + 3.2457x$ with $\mathrm{R}^2 = 0.9996$

Butyraldehyde $y = 0.6582x^3 - 1.4034x^2 + 4.3347x$ with $\mathrm{R}^2 = 0.9984$

Propionaldehyde $y = 0.6259x^3 - 1.1882x^2 + 2.7870x$ with $\mathrm{R}^2 = 0.9997$

3.3.2 Selection of the Cooling unit

The second important part of the overall apparatus is a suitable cooling unit, which, in addition to the providing the ability to cool, must be internally resistant to chemicals and must ensure air removal from the interior. Furthermore, openings must be provided to allow the necessary tubing to be inserted. The refrigerator should also have a window to allow visual checks to be carried out without interrupting operation. Additionally, the unit should be as compact as possible to keep the dead volume as low as possible. These requirements are met by the high precision climate chamber SU-242 from Espec. This chamber guarantees a temperature control of ±0.3 °C in a range from -40 to 150 °C. Position of the openings were placed with respect to our request to fulfill the required criteria for the desired application.

3.3.3 Vaporization unit selection

For the last part of the vapor generation system, i.e., the evaporator with dilution unit, no suitable commercial product was available. The idea here is to use a split/splitless injector of a gas chromatograph as a stand-alone device for this task. The company Gerstel was able to modify a programmed temperature vaporizing injector according to our given requirements. The Auxiliary Electronic Pressure Control (AuxEPC) as a stand-alone device for external use of the injector is already commercially available from Gerstel in the form of the controller C305. The modifications only affect the injector itself. The injector receives a custom-made, thermally insulated housing and a specially manufactured injector head. To obtain the desired concentration in the test gas facility from the dosed amount of analyte in the single-digit µL/min range, only a small portion of the vaporized analyte is added to the test gas stream; the remaining, considerably larger portion is discharged through the split outlet. Thus, there is no dilution of the dosed analyte quantity; rather a division of the vaporized analyte stream, as used in the split/splitless technique in gas chromatography, is affected. The alternative to injecting an analyte or sample into the injector with subsequent gas chromatographic analysis is continuous injection and vaporization. To ensure this, an injector head had to be built into, which the lines of the dosing system can be inserted without having to subject them to a restriction, e.g., in the form of a thin needle, as this would result in an undesirable increase in pressure. Based on these requirements, a direct injector head is converted and provided with a split outlet. The entrance to the evaporator is via a Swagelok connection. In order to achieve a direct change of the flow rate, the individual channels are first brought together in the injector head. This means that currently three pieces of tubing are led separately through a septum in the Swagelok connection directly into the hot zone of the injector. This type of injection is not used in gas chromatography and therefore was specially designed for the dosing system. A deactivated fused silica capillary column is used as retention gap column (see Table 4) and serves as an output to the test gas facility. The control of the gas flows is done by calculating the dimensions, e.g., the restriction of this retention gap column and the applied head pressure of the injector, as is done when using an injector in the GC. The maximum achievable dilution thus depends on the dimensions of the retention gap column. The head pressure of the injector must be selected so that p(pressure pump per channel) > p(head pressure in injector). Otherwise, the head pressure applied in the injector ensures that the analytes are no longer transported to the injector but are pressed back into the reservoir. At the pumps maximum control range of 1000 mbar, the EPC head pressure must not exceed 800 mbar. This leaves a control range for the pump of 200 mbar for conveying the analytes. Therefore, it is necessary that the pressure required for stable delivery of the desired flow rate is as low as possible under atmospheric pressure at the outlet (compare to Chapter 3.3.1). The choice of a small, stable flow rate allows a higher EPC pressure, and therefore a higher flow rate through the retention gap to the test gas facility.

The following Table 4 shows a selection of possible retention gap columns and the possible settings of the flow rates towards the test gas path and the maximum achievable split flows.

Table 4: Selection of retention gap columns and achivable flow settings.

Retention gap columns		EPC head pressure [mbar]	flow rate [mL/min]	average velocity [cm/s]	maximum split flow [mL/min]	maximum Split ratio
length [m]	inner diameter [µm]					
2	100	800	0.5	70.2	350	700 : 1
		200	0.1	18.8	99.9	999 : 1
1.7	320	100	6.2	121	99.9	56 : 1
		400	25.5	437	99.9	13.7 : 1
		500	33.0	541	350	10.6 : 1
2	530	100	39.1	281	350	8.9 : 1
		200	77.2	529	350	4.5 : 1
5	530	100	15.7	113	350	22.3 : 1
		200	30.9	212	350	11.3 : 1
5	320	110	2.3	45	350	152 : 1
		800	19.9	288	350	17 : 1

3.3.4 The combined dosing device

The following figure summarizes the developed concept for the dosing of substances with high vapor pressure (Figure 17). This is followed by a picture of the overall system (Figure 18).

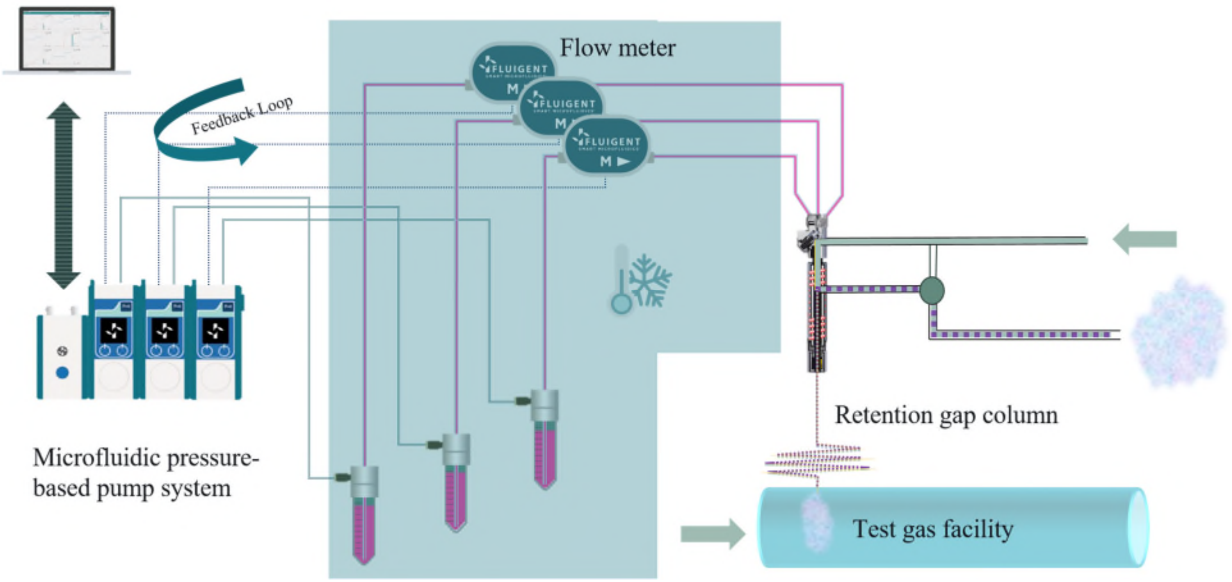


Figure 17: Concept of a dosage system for liquid substances with high vapor pressures. Microfluidic pressure pump, cooled sample path and programmed temperature vaporizer [62]

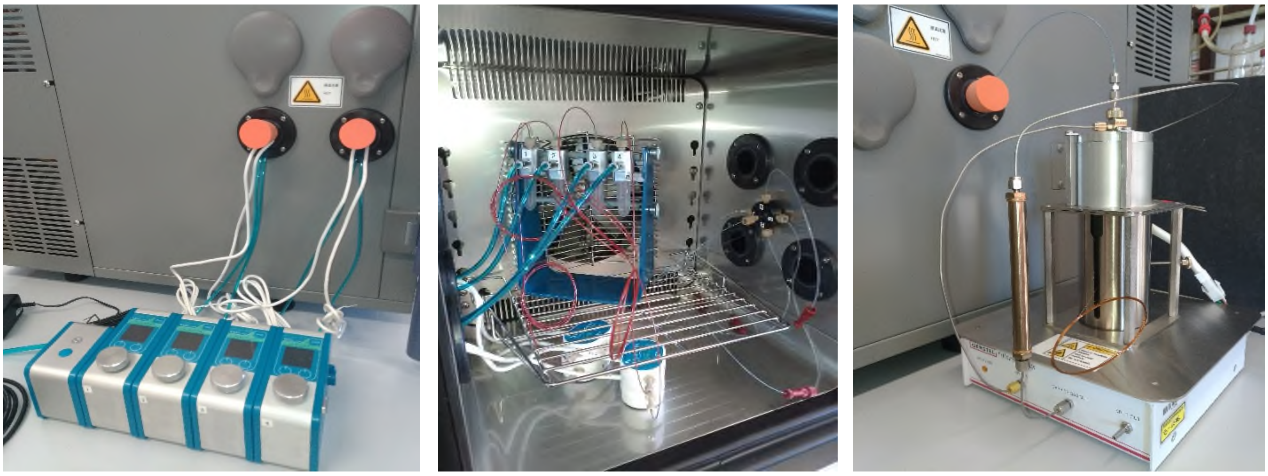


Figure 18: Pressure based dosage system for substances with low vapor pressure. Left: flow controller for pressure-based fluid control (FlowEZ™), middle: climate chamber with substance reservoirs and flow units inside, right: stand-alone Programmed Temperature Vaporizer

With the requirements and limitations described in Chapter 3.3.1 and 3.3.3, the appropriate retention gap column for experiments is selected based on the required concentrations of the test gases.

Calculation of the required dosage rate is based on the following settings during the proficiency test:

- Basic gas stream: 67 L/min
- Concentration range per analyte: 0.1 – 3 mg/m^3

Densities of aldehydes required for conversion:

- ρ (acetaldehyde) = 0.79 mg/µL
- ρ (butyraldehyde) = 0.81 mg/µL
- ρ (propionaldehyde) = 0.80 mg/µL

Dosing range in µL per aldehyde, which must enter the test gas facility per minute to cover the required concentration range:

Acetaldehyde	0.00845 µL – 0.2535 µL
Butyraldehyde	0.00838 µL – 0.2513 µL
Propionaldehyde	0.00827 µL – 0.2481 µL

Taking into account the minimum stable dosing rate of aldehydes and the requirement of equal concentrations in the test gas, butyric aldehyde determines the limiting factor of a minimum dosing rate of 2 µL/min (see chapter 3.3.1). The required split ratios for $c = 0.1\ mg/m^3$ and $c = 3\ mg/m^3$ per aldehyde at a minimum dosing rate of 2 µL/min/aldehyde are shown hereafter:

$$\left.\begin{array}{l} 6\ \mu L/\min \xrightarrow{Column} 0.025\ \mu L/min\ \ (aldehyde\ flow\ to\ test\ gas\ facility) \\ \\ \qquad\qquad\ \xrightarrow{Split} 5.975\ \mu L/\min\ \ (Surplus\ through\ Split\ outlet) \end{array}\right\} \begin{array}{c}\text{Split ratio}\\ 239:1\end{array}$$

The required split ratio for $c = 3.0\ mg/m^3$ per aldehyde:

$$\left.\begin{array}{l} 6\ \mu L/\min \xrightarrow{Column} 0.75\ \mu L/min\ \ (aldehyde\ flow\ to\ test\ gas\ facility) \\ \\ \qquad\qquad\ \xrightarrow{Split} 5.25\ \mu L/\min\ \ (Surplus\ through\ Split\ outlet) \end{array}\right\} \begin{array}{c}\text{Split ratio}\\ 7:1\end{array}$$

In order to cover the concentration range required for the proficiency test, from the selection of retention gap columns in Table 4, only the column with the following dimensions is considered: 2 m × 100 µm (inner diameter). Consequently, all following experiments are performed with this retention gap column.

3.4 Measurement equipment for online control of test gases

To obtain information about the quantitative composition of the analyte concentration during experiments respective to the proficiency tests, the application of online analytical methods is essential. For this purpose, two selective analytical methods are used. For online analytical control of VOC´s (concentrations in µg/m³ range) and solvents (concentrations in mg/m³ range), a modified gas chromatograph is in operation and gives quantitative results every seven minutes for experiments with solvents in the mg/m³ range, and every 21 minutes for VOC´s in the µg/m³ range. Differences in the analysis time are justified by different injection techniques, which are described further in Chapter 3.4.1 and 3.5.2.

Selected ion flow tube mass spectrometry (SIFT-MS) additionally creates the possibility to measure changes in concentration in real time. Within this thesis, this technique is used during experiments with VOC´s in the µg/m³ range and the quantification of aldehydes. Due to its quantitative measurement in real time, contributions to dosing errors, such as air bubbles in the tubing of the syringe doser and boiling delays, can be seen immediately and offer the opportunity for adjustment during the experiment. This is a huge advantage compared to offline measurements, where in the worst case the whole experiment has to be repeated; especially for proficiency testing schemes with participants, such a scenario would be a major trouble.

Apart from information about the quantitative composition of the test gas, environmental parameters such as air pressure, temperature and relative humidity are continuously measured and recorded with the ALMEMO® 2690-8 data logger. A manual gas meter measures the actual gas flow under the prevailing conditions. Thus the concentration can be calculated even more precisely afterwards.

3.4.1 Gas chromatographic system for online analysis

An online gas chromatograph (*Agilent 7890B*) with three columns and three injection methods is coupled to the test gas facility. Measuring gaseous samples requires a specific valve switching setup. The modifications of the commercial *Agilent 7890B* gas chromatograph were carried out by the company *Teckso solutions* and allow for the measurement of gaseous samples as well as liquid samples. An overview of the arrangement of the modified gas chromatograph with explanatory note about the use of the channels for online analysis is shown in Figure 19.

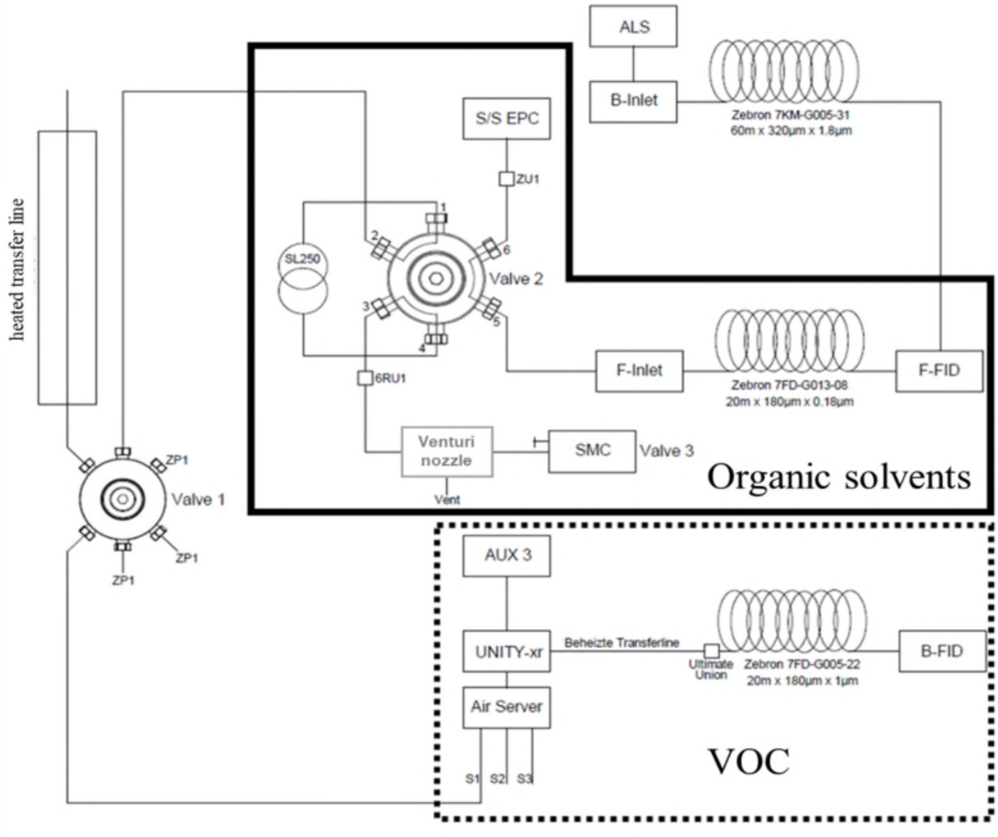


Figure 19: System drawing of the online gas chromatograph. [63]

3.4.1.1 Sample loop

One channel is used during the experiments with organic solvents in the concentration range of mg/m³. Because of the high analyte concentration, the test gas must not be enriched to achieve quantitative results above the required limit of quantification. The injection method used in this case is a sample loop with a volume of 250 microliters, which is filled by using the venturi nozzle of the chromatograph.

3.4.1.2 Thermal desorption pre-concentration

For the analysis of organic vapors (VOCs) in the µg/m³ range there exists the need for sample pre-concentration due to the low concentration of the test gas. For enrichment of the sample gas, a thermal desorption unit (TDU) is used. The Markes *AirServer-xr* inlet for gaseous samples is therefore coupled with a thermal desorber *UNITY-xr*. Because the test gas facility runs under atmospheric pressure conditions, the sample has to be actively suctioned out of the facility with an external pump. After passing through valve one (Figure 19), the sample gas is transferred unheated to the TDU where it is enriched on quartz Cold trap *General Purpose Carbon*, designed for hydrocarbons with a chain length between 4 and 30, what largely corresponds to the collection range of Tenax TA®. The arrangement of the TDU *Markes AirServer-Unity-xr* for the analysis of VOC´s in low concentrations is shown below in Figure 20.

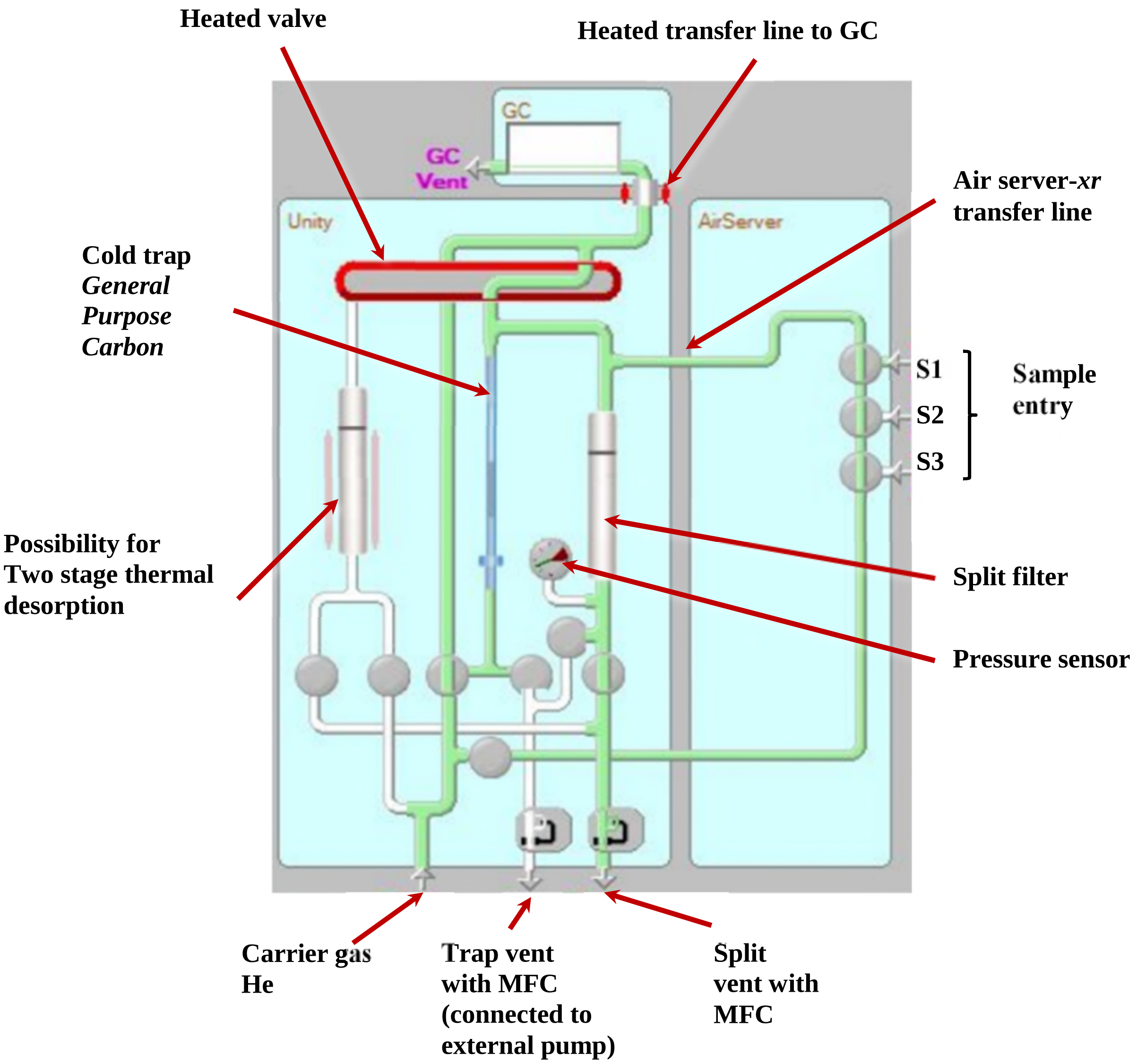


Figure 20: Sample path through Markes air server-xr coupled with thermal desorber UNITY-xr [64]

Before each sample collection, the tubing in the TDU is automatically flushed with carrier gas to avoid carry over, checked for leaks and pre-rinsed with sample to avoid dead volume. During sampling, the cold trap is flushed with sample and drawn in to the *AirServer-xr* by the external pump, in the direction of the trap outlet (collection direction). The cold trap can either been used at room temperature or cooled down by a Peltier element. Attainment of temperatures down to -30°C is possible. After collection, the cold trap and the sample path is flushed with carrier gas (Helium) in order to clean the cold trap of residues of air, especially oxygen, as well as moisture. Carrier gas supply is provided via an auxiliary pressure controller of the GC and is regulated by a metering valve and a pressure sensor operating in a feedback loop. After line flushing with carrier gas, the cold trap is heated to the desorption temperature with up to 100 °C/s and kept at the target temperature until the desorption phase ends. Information about chosen temperatures of the method is given in the experimental and results sections (4.2 & 5.1.2.2). If requested, desorption flow can be diverted via the split outlet to split out excess sample. An activated carbon filter cleans the exhaust air and a mass flow meter is installed at the split outlet to monitor the split flow. Once desorption is done and the sample has entered the GC, the cold trap is cooled down and a new cycle can be started while the desorbed sample is analyzed in parallel. This enables an even faster analysis time. Details on the gas chromatographic parameters for the analysis of organic solvents and VOC´s are given in Chapters 4.1.1, 5.1 and 5.2.

Independent of the online analysis, samples can be injected onto a third column using an auto sampler. This has not been done during the experiments in this thesis.

3.4.2 SIFT-MS in use for real time measurement of hazardous substances

SIFT-MS, compared to the oft-used GC-Setup, delivers quantitative results in real time. This means that for low concentrations in the µg/m³ range and even lower there is no need for preconcentration. This enables to monitor a startup profile and get a visual and analytical starting point for sampling every time. Furthermore, dosing errors, which usually take place at the run-in period, can be seen right away. During the offline sampling, SIFT-MS constantly records quantitative data, so that a gapless data set is available at the end of each proficiency testing scheme. This provides protection against potential doubts on the test gas by participants and, in addition, in case of uncertainty in the result, there is certainty that the error is not due to the test gas production.

Furthermore, real time data obtained by SIFT-MS can be used to observe the behavior of a new substance introduced in the test gas facility, e.g., its wall absorption behavior.

Since the device configuration is already described in Chapter 2.2.1, the connection to the test gas facility is shown below in Figure 21.

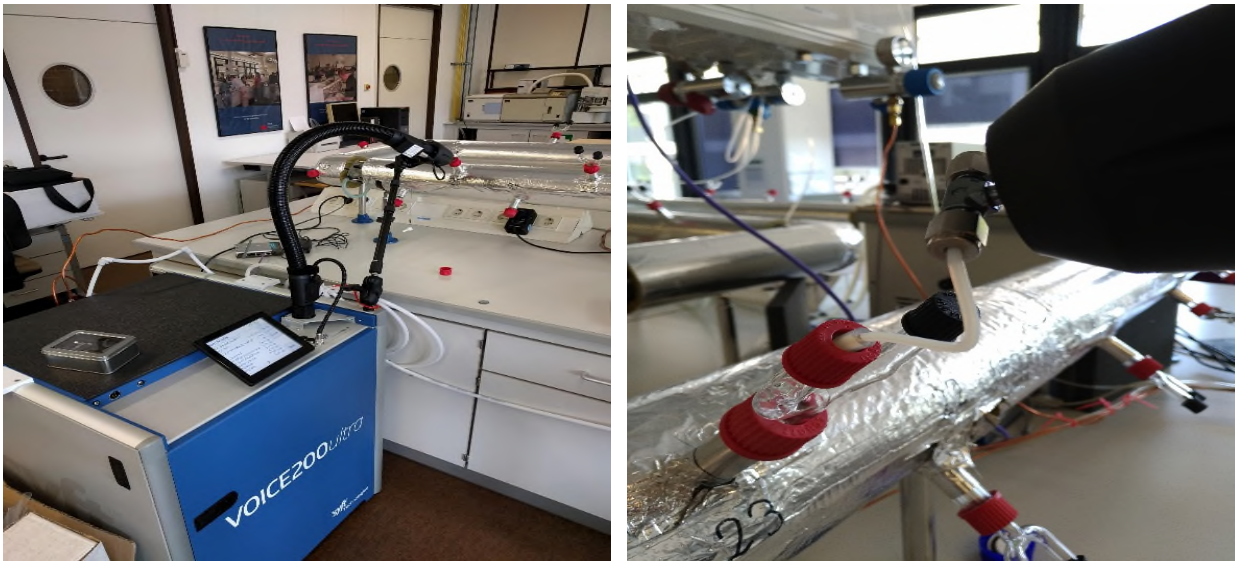


Figure 21: SIFT-MS Setup at the IFA, left: connection to the facility enlarged.

3.5 Analytical Methods

In the methods section, the basic steps of method development and validation are presented and explained. In particular, the section describes the method development and validation protocol for the online analysis of VOCs and organic solvents by means of gas chromatography. The method development and validation steps of the SIFT-MS methods for the quantitative online determination of VOCs and aldehydes during proficiency testing schemes are also covered.

3.5.1 Selected analytes of interest for occupational safety and health

The selection of the substances to focus on are dependent upon the substances that are relevant for occupational health and safety and which are possible to dose and vaporize with the available equipment. In the case of VOCs and organic solvents, which are dosed and evaporated with the Injection dosing pump HovaCAL® digital 321-SP (for details see Chapter 3.2.1), these are thermally stable substances with a boiling point below 170 °C. This limit results from the experience with the dosing unit and the maximum temperature of the vaporizer.

The situation is different for aldehydes. Since the focus here is on the development of the dosing unit, the selection of the substances is based on those compounds that are used during the proficiency testing scheme. These are formaldehyde (dosed by means of a permeation oven), acetaldehyde, butyraldehyde and propionaldehyde.

3.5.2 Quantitative gas chromatographic online analytical methods for VOC´s and organic solvents

In this chapter, the general procedure of method development for quantitative online analysis of VOCs and organic solvents in online controlled dynamic test gases is explained.

3.5.2.1 Column selection

To ensure the shortest possible analysis time, short (but efficient) columns are selected in the column selection process. The dimensions of the capillary columns Zebron ZB-624 (VOC analysis) and Zebron ZB-WAXplus (organic solvents analysis) used in this work are 20 m length and 0.18 mm in diameter (narrow-bore). The stationary phase of Zebron ZB-624 is composed of 6%-cyanopropylphenyl and 94%-dimethylpolysiloxanes and is, therefore, of medium polarity. The stationary phase of Zebron WAXplus is made of cross-bonded polyethylene glycol and is therefore polar (see Figure 22).

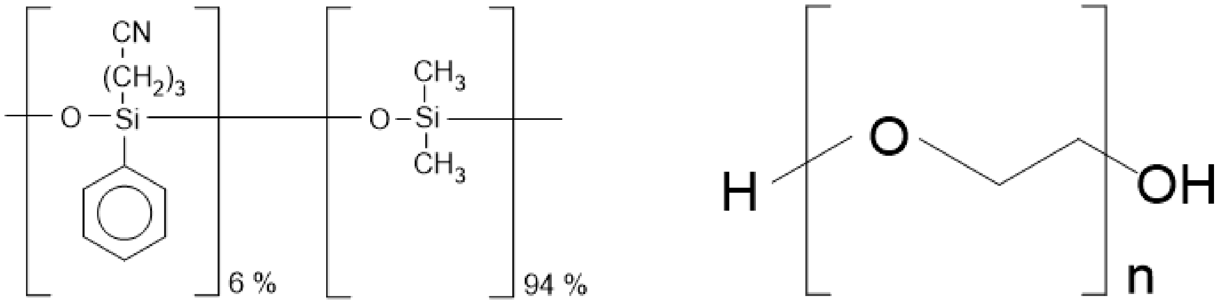


Figure 22: Composition of the stationary phase of Zebron ZB-624 with 6%-cyanopropylphenyl and 94%-dimethylpolysiloxane for analysis of VOCs (left) [65] and the stationary phase Zebron WAXplus (right) Crossbond polyethylene glycol. [66]

Both columns are designed for fast analysis and can be classified in the marginal range of fast-GC. The advantages of a narrow column compared to a column with normal diameter (0.2 - 0.32 mm) are increased separation performance and resolution (high number of theoretical plates), so that in combination with a shorter column, consistent results can be achieved in a shorter analysis time. The selection of the separation phase is based on EPA applications and the recommendations of the column manufacturers. [67, 68]

3.5.2.2 Steps for method development and validation

After selecting the separation phase, method development and validation takes place. For method development, first the method parameters are optimized in terms of analysis time, separation and sensitivity. Modified parameters are:

- Carrier gas flow or respectively carrier gas velocity
- Temperature gradient
- Split flow

Only when these aspects have been investigated, the elution sequence and thus the retention times of the substances are determined.

Regarding the method for the determination of test gases in the µg/m³ range, due to the use of the thermal desorption unit, further instrument parameters must be assessed in addition to the settings on the gas chromatograph:

- collection volume
- desorption time
- desorption flow
- temperature of the cold trap during the collection and desorption phase

The validation of the methods include calibration, regression analysis, determination of the limit of quantification and detection, selectivity, specificity, checking on accuracy with independent methods, precision, and robustness with regard to changes in humidity.

3.5.3 Method development for quantitative real time analysis of VOCs and aldehyde test gases with SIFT-MS

When it comes to SIFT-MS method development, it differs from the method development of chromatographic methods. The usual approach cannot be applied and must be adapted while keeping guidelines for conventional techniques in mind.

Therefore, the specificity of the method is shown by searching the SIFT-MS library to assess any potential product ion conflicts that may occur with other volatile compounds. Analyzing the instrumental background completes the demonstration of specificity. To evaluate linearity the signals are plotted as a function of analyte concentration. For conventional techniques, e.g., gas chromatography, this means plotting the peak area or height versus the calculated concentration; for SIFT-MS the measured concentration is plotted versus the calculated concentration and checked to see if the measured concentration reflects the concentration in gas. For the method development in this thesis, linearity is given if all recoveries are 100% ± 20%.

Tests on precision are done similar to precision testing in the gas chromatography method validation. Six measurement of three preparations at ~ 50 % of the linear range are conducted. Preparations are made independently from the calibration preparation or mixture. The relative standard deviation of the measurements is calculated to assess precision. Intermediate precision is established due to the circumstances that the measurements are intended to be made by different analysts at the institute. This procedure establishes the effects of random events on the precision of the analytical procedure. Compared to a conventional technique, such as liquid or gas chromatography, there is no need to check on effects as fresh diluent or different column. For accuracy, spiking samples with the analyte and calculating the recovery of the spiked versus the un-spiked sample is a common method. For SIFT-MS spiking is not practicable. Additionally, offline measurements with independent, validated methods are done and compared to the SIFT-MS obtained results. The evaluation of robustness should show the reliability of an analysis with respect to variations in the sample, as humidity. In addition, robustness has to be evaluated for uncontrollable system parameters that change from day to day. Both the temperature of the sample inlet and the prevailing temperature in the flow tube could affect the methodology of the system (see equation 1.15). If the temperature of the sample inlet changes, this could affect the concentration as the sample flow into the system would be affected. Also the temperature in the flow tube where the reactions take place can theoretically have an influence on the concentration. As a reminder, the reactions between the analyte and the reagent ions occur at a fixed reaction rate; as the temperature changes, the reaction rate may change slightly. The system has control of these heated zones but there is a tolerance of plus or minus seven degrees C from the set point. To find out whether the temperature of the inlet within the tolerance has an influence on the result the precision test is repeated at ~50 % of the linear range with different flow tube and inlet temperatures between ± seven degrees from its set point and comparing the recovery. The limit of quantification and the limit of detection is determined by the signal-to-noise ratio.

3.5.4 Use of independent offline methods for accuracy testing

To ensure the results of the quantitative online methods in the validation process with regard to accuracy and correctness, independent, validated offline methods are used. Therefore, an active sampling of the test gas is performed. For this purpose, the test gas is passed over a collection medium, which adsorbs the analytes. According to the applied analytical method, the analytes are desorbed and made available for analysis.

A multi-channel sampling system from Analyt MTC is used to load the sample carriers. Six sample carriers are loaded in parallel. Figure 23 shows the practical setup exemplar for collecting VOC samples on thermal desorption tubes.

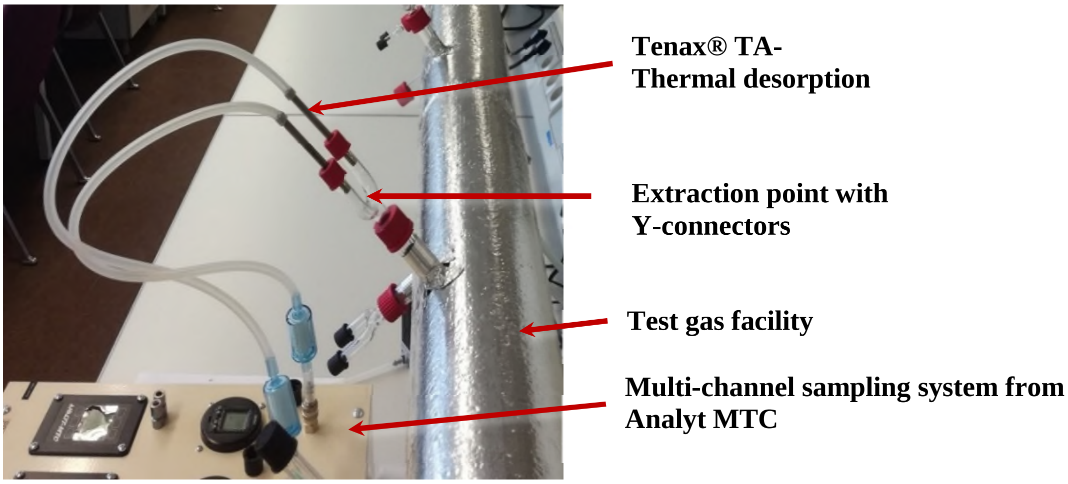


Figure 23: Setup for loading sample carriers at IFAs test gas facility.

For the offline TD-GC-MS method for the analysis of VOCs, the sample collection is done on Tenax® TA thermal desorption tubes. The analytical method to determine the VOC concentration on the sample carrier is an already validated and established method for the determination of VOCs in the air at the workplace. A detailed description of the method can be found in the IFA workbook. [69] For the offline analysis of aldehydes, sampling takes place on cartridges filled with 2,4-dinitrophenylhydrazine (DNPH) impregnated silica gel, see Figure 24.

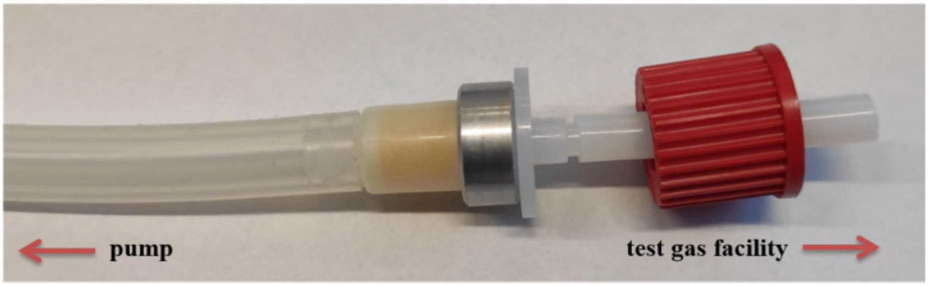


Figure 24: Connection of the aldehyde collection phase Waters Sep-Pak XPoSure to the test gas facility

DNPH acts as derivatization agent and converts the aldehydes to the corresponding hydrazones (Figure 25). After elution with acetonitrile, the determination of the aldehydes is performed by high performance liquid chromatography (HPLC) with diode array detector according to the IFA workbook (key figure 6045) [70].

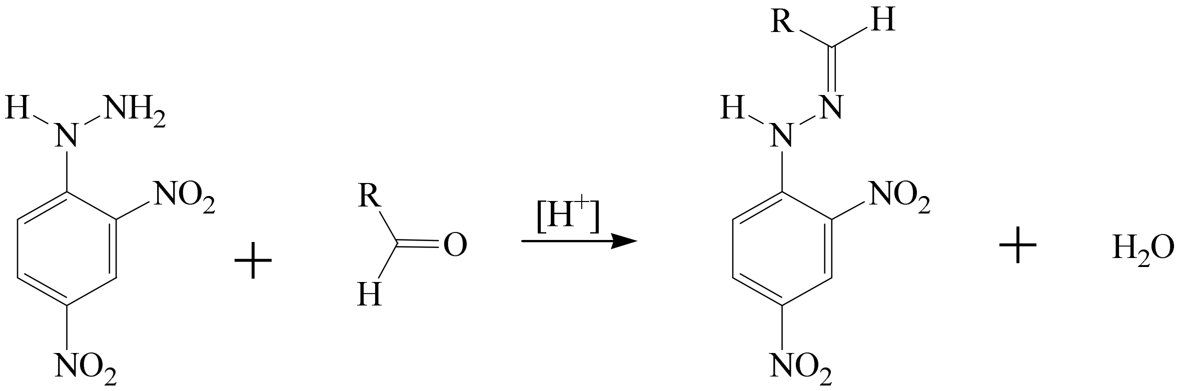


Figure 25: Reaction of aldehydes to hydrazones using DNPH cartridges [71]

4 Experimental

This chapter explains the experimental procedure for method development and validation of the different online measurement methods. For the method of VOC determination, the procedure for determining the retention time, the optimization of the separation performance and desorption efficiency, the influence of humidity and the individual validation steps are explained. Similarly, the description of the development of the measurement method for organic solvents is also given. For the validation of the SIFT online measuring methods for VOCs and aldehydes, a different procedure is used, which is also described in this chapter.

4.1 Method development for gas chromatographic online analysis of VOC test gases and organic solvent test gases

In this section, the development of gas chromatographic methods is explicitly discussed. Since the procedure for method development for the determination of VOCs and organic solvents is very similar, this will be summarized as far as possible and differences in the procedure will be indicated.

4.1.1 Determination of the method parameters for gas chromatographic separation

When developing the online-GC methods, experiments have been first carried out for the chromatographic separation of the substances. Since the methods differ with regard to the structure of the apparatus (see Section 3.4.1), the description of the procedure for achieving the optimal parameters for separation is described individually in the following.

4.1.1.1 Determination of the method parameters for online VOC measurements

The first approach to develop suitable method parameters has been carried out by a master student who was supervised in the context of this thesis. The results of this are listed in the results section in Chapter 5.1. The process to the determination of the method parameters can be read up in the master thesis. [72] In a second approach, the chromatographic method was slightly revised for possibly better separation and shorter runtime for use during the proficiency testing scheme. The procedure is described further below.

In the method for online VOC test gas determination, it is necessary to define parameters for the thermal desorption when optimizing the separation efficiency. Some parameters have a direct influence on each other and have to be adjusted to each other. For example, the desorption time must not exceed the holding time of the initial GC oven temperature as long as desorption and sample transfer have not been completely accomplished. Consequently, the initial temperature of the GC oven program must be maintained during desorption phase. Otherwise, there may be insufficient focusing at the beginning of the column. This means that less strongly adsorbed VOCs, mostly the more volatile VOCs, are already transported a little bit through the column by the carrier gas due to the early rise of the oven temperature, while less strongly adsorbed, or less volatile, VOCs have not yet entered the GC or have not yet been desorbed. Thus, the less volatile VOCs are affected by peak broadening as observed by Sanchez and Sacks [73] in thermal desorption experiments on an uncoated capillary column.

In the case of online analysis, special attention should be paid to the time factor and the avoidance of memory effects by carryover. In the case of continuous online analysis, where one analysis follows the next, even very small carry-overs would become noticeable and add up over time. It is therefore essential to find the shortest possible desorption time to ensure no sample remains on the cold trap.

As already mentioned before, the Zebron ZB-624 column is used for separation of the VOC test gas. The length of the column is only 20 meters and it is designed for fast analysis and can be classified in the marginal range of fast-GC analysis. The advantages of a narrow column are increased separation performance and resolution, so that in combination with a shorter column, consistent results can be achieved in a shorter analysis time. Not only the length of the column contributes to a shorter analysis time, a high carrier gas flow is also beneficial and is usually used in fast GC methods [74]. In the case of thermal desorption, also the desorption efficiency increases by increasing the desorption flow. This has been confirmed by Woolfenden in 2012, [75] who showed that doubling of the desorption flow allows approximately a halving of the desorption time with the same desorption efficiency.

The manufacturer's recommendations for the Flame ionization detector have been adopted. The hydrogen supply is 30 mL/min and the air supply at 300 mL/min is ten times as much. To minimize the risk of water condensation in the detector, a detector temperature of 300 °C is set. The column flow is increased to 5 mL/min using helium as make-up gas. As starting point for the method development, the US EPA method 8260D [76] is used and the following parameters have been adjusted to achieve the best possible separation in the shortest possible run time:

- Column flow
- Temperature program
- Sample volume
- Desorption split

Details of the procedure are explained in the results section (5.1.2).

4.1.1.2 Determination of the method parameters for online analysis of organic solvent test gases

For test gases of organic solvents in the mg/m³ range there are fewer parameters to optimize because of the absence of the thermal desorption unit for pre-concentration. For this method, the focus is on the carrier gas flow, temperature gradient and split flow to find the optimal settings for best separation and sensitivity over the analyte concentration range during proficiency testing, taking the analysis time into consideration.

4.1.2 Retention time determination

Since no mass spectrometer is available for the identification of the components, the selected analytes have to be injected once at a time to determine their retention times. A gasbag filled with air is used for this purpose, into which the substances are injected one after the other. The gasbag is not cleaned between the injections, so that a new peak is added to the chromatogram with every analysis, which can be assigned to the previously injected substance. The gasbag is only used for qualitative purposes during this operation.

4.2 Validation of the online-TD-GC-FID method for VOC test gases

The evaluation of the process characteristics such as the limit of quantification, the working range and the influence of humidity were investigated within the scope of a master thesis. A detailed description of the working steps can be found there. [72] The experiments and their results are summarized below.

4.2.1 Calibration

A ten-point-calibration in the concentration range 5-250 µg/m³ has been performed. Three measurements were performed for each calibration level. Six measurements were performed for normal distribution, precision and variance homogeneity at a low, two intermediate and one high concentration. The evaluation is performed by plotting the measured peak areas against the target concentration.

After evaluation of the ten-point calibration, a further calibration is carried out in the range of the limit of quantification to determine the limit of quantification (LOQ) regarding to DIN 32645. [77] This calibration is carried out with six calibration points but also here a triple determination is carried out.

4.2.2 Quality control samples

After calibration, a test gas containing all 23 calibrated analytes is generated, which is quantified with the online measurement method as well as with a validated offline-TD-GC-MS method. For co-eluting analytes the sum of the values is used to determine the recovery. A total of four test gases with different concentrations of the individual analytes are produced. By means of the online method, three values are obtained; the offline analysis is done by double determination. Offline sampling was performed over two hours with a flow of 66.6 mL/min on Tenax®-TA sample carriers. [69]

The results of the multiple measurements are averaged and the recovery of the two methods is calculated. The calculated target concentration is taken as the true value. Since the offline method is a validated method, the correctness of these results is assumed. Thus, by measuring the quality control samples, conclusions can also be drawn about the correctness of the online method.

4.2.3 Influence of sample humidity

Seventeen of the separable analytes of the online VOC method are tested on the influence of humidity based on the recovery rate. A test gas with a concentration of 90 µg/m³ per analyte is generated for this test. The relative humidity is set to four humidity levels via the humidifier unit of the test gas line: 19.1±0.2 %, 40.4±0.4 %, 60.1±0.5, 81.7±0.9 %. For comparison, calibration and measurement of the quality control samples were carried out at a humidity of 34 %, which usually corresponds to the humidity set during a proficiency test.

4.3 SIFT-MS method development

Within the scope of this work two SIFT-MS methods for the online control of test gases are developed. One method is used for quantitative monitoring during the VOC proficiency test in addition to the gas chromatographic online analysis. Furthermore, SIFT MS is used for the continuous quantification of aldehydes during the development of a new dosage system for generating aldehyde test gases for proficiency testing purposes. For aldehyde test gases in the test gas facility of the IFA, the analysis by SIFT-MS is the only specific online control available in addition to offline-HPLC analysis, which is traditionally used for quality assurance in the proficiency testing scheme. In the following, the general procedure of a method development for SIFT-MS is described. It should be noted that the development of SIFT-MS methods is very case specific and only an insight into the basic procedure is given here.

4.3.1 General aspects of SIFT-MS method development

After ensuring that the target compounds are entered in the library, instrument parameters such as scan time and measurement limits are set. These settings are slightly modified and optimized later. After that, the selection of the target compounds from the compound library is implemented. Then, the most critical step of resolving target compounds takes place.

First, it is checked whether there is at least one analyzable mass for each substance of the method that does not interfere with the mass of another substance. If there is even more than one unique product ion, preference is given to quantifications with a fast reaction rate (k>1.0E^{-9}) and a branching ratio of at least 20%. If unique product ions can be identified for the individual analytes, this is the simplest case in this process and the method can be tested under real conditions.

Table 5: SIFT-MS example of overlap with different reaction rates. [78]

Compound	Reagent ion	Reaction rate k [cm^3 molecule^{-1} s^{-1}]	Branching ratio [%]	Mass (m/z)	Product	Scan	Calculate
Dimethyl sulfide	NO$^+$	2.2E^{-9}	100	62	$(CH_3)_2S^+$	✓	✓
Methanol	NO$^+$	1.0E^{-11}	100	62	NO^+•CH_3OH		
Example: Methanol reacts very slowly with NO$^+$, so the dimethyl sulfide product can usually be retained.							

In case of complete overlap with the reaction products of other analytes, quantification can be done as a sum of the analytes, or further investigation can be done to allow quantification of the individual analytes. This depends on the research question. If further attempts are to be made for selective quantification of the analytes, a closer look is taken at the interfering masses. This includes the identification when apparent overlaps are not an issue. This is the case if the analytes react with the corresponding reagent ion at different rates, respectively if one of the analytes reacts only very slowly with the reagent ion while the other analyte has a very fast reaction rate. Table 5 shows an example for such a case.

Another example of interfering products with low influence is shown in Table 6. Here both analytes react rapidly with NO^+, but the butanol product, which interferes with propionaldehyde has a very small branching ratio. Therefore, the propionaldehyde product can be retained in this case as well.

Table 6: SIFT-MS example of overlap with different branching ratios. [78]

Compound	Reagent ion	Reaction rate k [cm^3 molecule^{-1} s^{-1}]	Branching ratio [%]	Mass (m/z)	Product	Scan	Calculate
Propanol	NO^+	$2.5E^{-9}$	100	57	$C_3H_5O^+$	✓	✓
1-Butanol	NO^+	$2.2E^{-9}$	5	57	$C_4H_9^+$	✓	✓
	NO^+	$2.2E^{-9}$	95	73	$C_4H_9O^+$	✓	✓
Example: The butanol product that interferes with propanal has a very small branching ratio. → propanal product ion can be retained							

These theoretical assumptions have to be verified in practice and only if the assumption is confirmed can the product be used for quantification. The same applies to the use of products with a low reaction rate or low branching ratios. Such products are usually not used for quantification if non-interfering products are available. It is to be noted that the use of products with these criteria results in much reduced sensitivity to the compound and greater susceptibility to any unforeseen interference (like false readings)! Therefore, quantification based on these reactions, respectively product ions should only be considered if other possibilities for quantification, such as the following, are not possible. In the case that all products of one analyte (A) interfere with another (B), but the latter (B) also has a unique product, a subtraction can be performed to calculate the individual concentrations. This possibility should also be checked for interfering substances in general.

4.3.2 SIFT-MS method development for VOC test gas monitoring

In this chapter, the method development process described in the previous chapter is applied and demonstrated in practice.

Since SIFT analysis during the VOC proficiency test is a complementary analysis to GC, the focus of SIFT analysis is on real-time monitoring, which the gas chromatographic method cannot provide, since there is a relatively long timespan between quantitative results. The SIFT analysis is primarily intended to confirm the homogeneity of the test gas during the experiment. Only in the second instance are quantitatively correct results of interest. Therefore, two SIFT-MS methods are used during the proficiency test. One method reproduces the concentration curve of the test gas over a period of 90 minutes. Thus, the time from which a homogeneous test gas is available can be optimally determined and any errors in the dosage are immediately visible. The second method is used as soon as the test gas is homogeneous and loading of the sample carriers begins. With this second method, quantitative results are obtained additionally to the one-GC results.

4.3.2.1 Selection of product ions

A list of all reactions available for quantification of the selected VOCs contained in the proficiency test is given in Appendix 1.

- Benzene, ethyl acetate and octane react with different reagent ions to form unique product ions in the existing matrix. These substances are therefore unproblematic in terms of method development. For the measurement of benzene all reactions stored in the library can be used for quantification. All reactions are fast ($k > 1.0 \cdot 10^{-9}$ cm^3 $molecule^{-1}$ s^{-1}) and the branching ratios are above 20% for all reactions.

- For octane, three reactions are available for quantification according to the library. However, the reactions of octane with H_3O^+ and NO^+ are rather slow with $k=9.0E^{-10}$ and $7.0E^{-10}$ cm^3 $molecule^{-1}$ s^{-1} respectively and therefore the reaction of octane and O_2^+ is selected for the quantification of octane.

- Ethyl acetate can be quantified over six different productions. However, two reactions (H_3O^+ and one of the O_2^+ reaction channels) cannot be used because the secondary product in the corresponding channel interferes with the masses of other analytes. As mentioned in 2.2.2, the corresponding secondary product should always be measured together with the primary product of a channel. Of the remaining four reactions that can be used for quantification, the reaction of ethyl acetate with NO^+ was selected because it is the fastest and reactions with NO^+ are only slightly influenced by humidity in contrast to reactions with O_2^+. [40]

For the remaining analytes in the test gas mixture, quantification by SIFT-MS does not involve unique product ions as described above, since the masses of the useful product ions interfere with masses of other analytes.

- In the case of toluene and α-pinene, here the so-called subtraction feature can be applied. A prerequisite for the application of this feature is that one of the analytes is quantifiable by means of unique product ions. In this case α-pinene is quantified by the reaction of H_3O^+ and the mass m/z=137 of the corresponding product ion $C_{10}H_{17}^+$ and additionally by the reaction with NO^+ and the corresponding ion $C_{10}H_{16}^+$ (m/z=136). For toluene, all resulting product ions interfere in their mass with α-pinene, which is why no quantification via a unique product ion is possible here. The subtract feature is applied here, which means that one of the toluene product ions is selected for quantification, but does not determine the actual concentration of toluene but the sum concentration of toluene and α-pinene. From this total concentration, the concentration of α-pinene determined by its unique product ions is subtracted to determine the toluene concentration. A subtraction factor is determined and written down in the method, so the calculation is automated.

- In the case of xylene and ethylbenzene, it is only possible to quantify them as a sum, since all resulting product ions of both analytes interfere.

- The same applies to 1,2,4-trimethylbenzene and cumene. However, cumene has a large number of resulting product ions, most of which, however, are only formed at a branching ratio of <20 %. These are normally not selected for quantification when other product ions are available. Since the product ions that are well suited for quantification but interfere with 1,2,4-trimethylbenzene, the quantification of the product ion $C_9H_{11}^+$ (m/z=119), which is formed by the reaction of NO^+ with cumene, is checked for its reliability before the decision of a total quantification is made. Unfortunately, it turns out that the product ion with a branching ratio of 15 % is not suitable for quantification. Therefore, a quantification as sum of the concentrations is performed for 1,2,4-trimethylbenzene and cumene.

An overview of the scanned masses for the measurement method to quantify the VOCs in the test gas mixture for the proficiency test 2019 are listed in Table 7.

Table 7: Scanned masses to quantify the VOCs in the test gas for the proficiency test 2019.

Compound	Reagent ion	Product
α-Pinene	NO^+	$C_{10}H_{16}^+$ [136]
	H_3O^+	$C_{10}H_{17}^+$ [137]
Benzene	NO+	$C_6H_6^+$ [78]
	O_2^+	$C_6H_6^+$ [78]
	H_3O^+	$C_6H_6.H^+$ [79]
Ethyl acetate	NO^+	$NO^+ \bullet CH_3COOC_2H_5$ [118]
Octane	O_2^+	$C_8H_{18}^+$ [114]
Sum 1,2,4-trimethylbenzene and cumene	O_2^+	$C_8H_9^+$ [105]
	NO^+	$C_9H_{12}^+$ [120]
Sum ethylbenzene and xylene	O_2^+	$C_7H_7^+$ [91]
Toluene	NO^+	$C_7H_8^+$ [92]

4.3.2.2 Calibration

To calculate the actual reaction rates, a 5-point-calibration was performed over the entire working range of 10-200 µg/m³. For the sum determination of ethylbenzene and xylene and 1,2,4-trimethylbenzene and cumene the working range extends to 20-400 µg/m³.

4.3.3 Development of a SIFT-MS method for monitoring aldehyde test gases

For the quantification of aldehydes in test gases the SIFT-MS technique is the only available online measurement technique at the IFA. The test gas mixture during the proficiency test contains four aldehydes (formaldehyde, acetaldehyde, propionaldehyde and butyraldehyde), which are to be quantified simultaneously and selectively. A list of all available reactions and the corresponding products can be found in the results and discussion section (Table 22). In the test gas matrix, all aldehydes can be selectively determined with different productions. With one exception (i.e., reaction with O_2^+ results in the production of $C_2H_4O^+$ with mass 44 for butyraldehyde and acetaldehyde) there is no interference of the productions. Even if some reactions are slow ($k<<1.0 \cdot 10^{-9}$ cm^3 $molecule^{-1}$ s^{-1}) or have a small branching ratio of <20%, all available reactions are selected for quantification and calibration. In the later course of method development (see results section), the reactions that are not or less suitable for quantification are sorted out.

5 Results and discussion

5.1 Validation results of the online analysis VOC method

In the following, the results of the validation of the online-GC method for quantification of VOC test gases are described. As already mentioned, a large part of the results is from a master thesis supervised in the context of this work.

5.1.1 Retention time determination

Currently 24 substances are identified for the VOC online method. A list is shown in Table 8.

Table 8: Compounds identified and calibrated for VOC online-GC-FID method.

Peak	VOC Compound	Retention time [min]
1	2-Butanone	3.926
2	Ethyl acetate	4.005
3	Benzene	4.859
4	2-Methoxyethanol	5.110
5	n-Heptane	5.201
6	1-Methoxy-2-propanol	5.869
7	n-Butanol	6.026
8	2-Ethoxyethanol	6.899
9	4-Methyl-2-pentanone	7.337
10	Toluene	7.430
11	1-Ethoxy-2-propanol	7.549
12	n-Octane	7.574
13	Butyl acetate	8.693
14	Ethylbenzene	9.543
15	m-Xylene	9.719
16	n-Nonane	9.769
17	α-Pinene	10.703
18	Cumene	10.805
19	2-Ethoxyethylacetate	10.811
20	Propylbenzene	11.061
21	2-Butoxyethanol	11.434
22	n-Decane	11.744
23	1,2,4-Trimethylbenzene	12.260
24	1,2,3-Trimethylbenzene	12.881

5.1.2 Optimizing the separation performance

As mentioned in the experimental part, the method development for online-VOC test gas monitoring was mostly carried out by a master student who was supervised in the context of this thesis. A more detailed description of the approach is given in this thesis. Nevertheless, the most important steps are described and presented below.

5.1.2.1 Chromatographic conditions

The establishment of the optimal separation parameters for gas chromatography described in the following differs slightly from those of the master's thesis. [72] Small changes in the temperature program and on the carrier gas flow have a positive effect on the separation. The adjustment of the method was carried out especially for the application during the VOC proficiency test.

As starting point for the method development, US EPA method 624 Volatiles on SPB-624 is used: 40°C (1 min), 11 °C/min to 125, 35°C/min to 230 °C (2 min) with carrier gas flow of 1.5 ml/min. For the thermal desorption method, the optimal parameters determined within the scope of the master thesis were applied (see 5.1.2.2).

First tests show that reducing the initial temperature to 30 °C has a positive effect on the separation of 2-butanone and ethyl acetate. Although the two components are not baseline separated at higher concentrations at this temperature, they can be determined semi-quantitatively next to each other. 2-butanone and ethyl acetate elute at 30 °C after about 4 minutes as first components. As mentioned before, the desorption time must not exceed the holding time of the initial GC oven temperature as long as desorption and sample transfer have not been completed. Otherwise, there may be insufficient focusing at the beginning of the column. This leads to a hold time of 3 minutes at the initial temperature of 30 °C. Re-desorption of the cold trap after sample transfer shows no memory effects, indicating sufficient desorption efficiency.

It is not yet possible to achieve sufficient signal separation under the selected settings, so the temperature program and carrier gas flow must be adjusted accordingly. Increasing carrier gas flow has a positive impact on the separation. **2.7 ml/min is determined as the optimum carrier gas flow for this method.** To adjust the temperature program to the chosen analytes, the first ramp is decreased from 11 to eventually 8 °C to get better separation. Heating the furnace from 8 °C/min to 100 °C turns out to be optimal. Reducing the temperature from 130 °C to 100 °C saves time and has no negative influence on the separation.

Since the last analyte (1,2,3-Trimethylbenzene) elutes shortly after reaching 100 °C, the maximum heating rate can be selected from this point on. Increasing the second heating rate to maximum temperature (65 °C/min) has no negative effect on the separation, but pushes the peaks together and shortens the running time. Heating up after all components of interest have eluted is necessary in order to flush any contaminants that may elute from the column later. A heating rate of 65 °C/min from 100 °C up to 155 °C is sufficient because no further impurities were visible in the chromatogram with extended oven program. For pure test gases in this boiling range no further impurities are to be expected. To be on the safe side, a short holding time of 1 minute is programmed for the relatively low final temperature of 155 °C. For all further proficiency testing schemes for VOC in this thesis the final temperature program is **from 30 °C (3 minutes) to 100 °C (0 minutes) at 8 °C/min, then to 155 °C (1 minute) at 65 °C/min,** which corresponds to an **analysis time of 13.6 minutes.** Further optimization of the separation performance, which would be associated with an extended analysis time, has not been carried out.

The chromatogram displayed in Figure 26 shows that most of the substances are separated during the run on the selected column. The substances 1-ethoxy-2-propanol and n-octane as well as cumene and 2-ethoxyethyl acetate cannot be selectively separated on the selected column taking into account the time component. The compounds thus cannot be quantified simultaneously during a proficiency test. Similarly, simultaneous determination of 2-methoxyethanol and heptane is only possible to a limited extent, since the signals are not optimally separated here either. Nevertheless, a separation can be observed and a quantitative statement is conditionally possible.

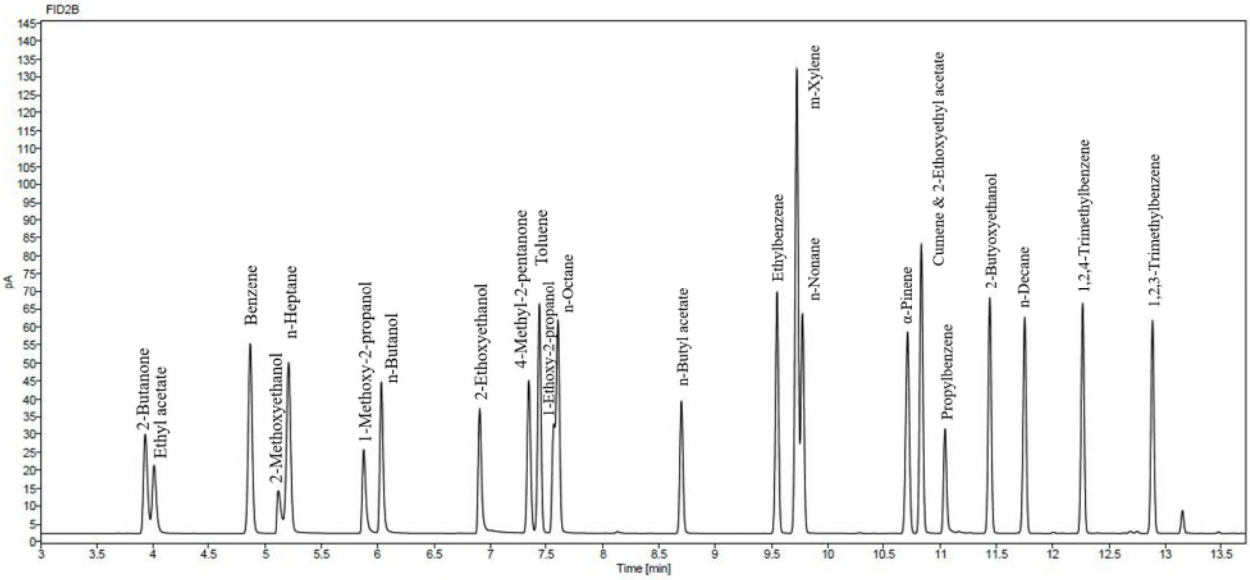


Figure 26: Chromatogram of the method for online VOC analytics. Concentration: 200 µg/m³

5.1.2.2 Thermal desorption

The setting of suitable method parameters for the thermal desorption aims at a complete desorption. An incomplete desorption does not only lead to a low recovery but also to carryover. Even small carryovers can interfere with the quantification of the subsequent measurement. To investigate a possible carryover, blank values are measured after the analysis of the test gas. For this the carrier gas is passed through the cold trap instead of the test gas. The influence of the following parameters was considered to achieve an efficient, complete desorption.

- Collection volume
- Desorption time
- Split flow

The choice of the desorption temperature is based on the manufacturer's recommendations of 300 to 320 °C. By choosing the high desorption temperature of 320 °C, an insufficient desorption due to a too low desorption temperature is excluded. During the collection phase, the cold trap is cooled to 10 °C. This is sufficient for the analytes used and their volatility and freezing of the cold trap due to the humidity of the sample is avoided. The heating rate during desorption process is set to the maximum. This could have a negative effect on the reproducibility due to varying ambient conditions, but this is eliminated by the constant air conditioning of the laboratory. Before desorption, the cold trap is flushed with carrier gas to remove oxygen and thus protect the column.

The parameters of collection volume, desorption time and split flow have been adapted to be used for the analytes with low response at low concentrations as well as for the analytes with high response at high concentrations with regard to quantification and carryover. The parameters for thermal desorption are determined during the master thesis and are shown in Table 9.

Table 9: Thermal desorption parameters of online VOC test gas monitoring by TD-GC-FID [72]

TD method parameters		
sample purge	sample purge time [min]	1
	split flow [mL/min]	50
sampling	sample time [min]	6
	sampling flow [mL/min]	50
line flush	line flush time [min]	1
	line flush flow [mL/min]	50
trap settings	trap purge time [min]	1
	trap purge flow [mL/min]	50
	trap low temperature [°C]	10
	trap heat rate [°C/s]	max
	trap high temperature [°C]	320
	trap desorb time [min]	3
	trap desorb split [mL/min]	15

5.1.3 Calibration and determination of the limit of quantification

Due to the co-elutions, the calibration is carried out in two approaches within the master thesis. The respective co-eluting analytes are quantified separately for the calibration. Since the use of co-eluting analytes is avoided during the proficiency testing schemes, this does not pose a problem in terms of quantification.

Preparation 1 contains ten analytes, preparation 2 contains 13 analytes in equal parts by weight, see Table 10. The limit of quantification was determined according to the calibration line method.

Table 10: Calibration approaches for the calibration of the VOC online-GC method.

Preparation 1	Preparation 2
Ethyl acetate	Butanone
2-Methoxyethanol	Benzene
1-Methoxy-2-propanol	Heptane
2-Ethoxyethanol	1-Butanol
4-Methyl-2-pentanone	Toluene
1-Ethoxy-2-propanol	n-Octane
Butyl acetate	Ethylbenzene
m-Xylene	Nonane
α-Pinene	1-Methylethylbenzene
2-Ethoxyethyl acetate	Propylbenzene
	n-Decane
	1,2,3-Trimethylbenzene
	1,2,4-Trimethylbenzene

The result of the calibration is summarized in Appendix 2. Further information on statistics can be taken from the publication of Kaus et al. [79]. In the following, only cases that deviate from the ideal are described in more detail.

2-Ethoxyethanol and 2-Ethoxyethyl acetate are examples for limitations of the linear working range. From the calibration data of 2-Ethoxyethyl acetate (Figure 27) it can be seen that the lower calibration levels (5, 10 and 20 µg/m³) produce a disproportionately small signal compared to the higher ones. The slightly different peak areas are primarily due to the background noise and not to the influence of the concentration. Only from a concentration of 40 µg/m³ onwards, an approximately constant response factor is observed. The response factor describes the ratio of the peak area to the concentration and is almost constant in a linear relationship. This already limits the working range for 2-ethoxyethyl acetate to 40-250 µg/m³ with seven calibration points, however without consideration of the limit of quantification. The negative axis intercept of the 7-point calibration also shows the late onset of the working range.

2-Ethoxyethyl acetate (I)

40 - 241 µg/m^3

Red calibration points in non-linear range

→ 7 calibration levels (n=3)

$y = 0.146x – 5.779$

$r = 0.9945$

$V_{x0} = 7.01$ %

LOD = 84 µg/m^3

→ invalid calibration

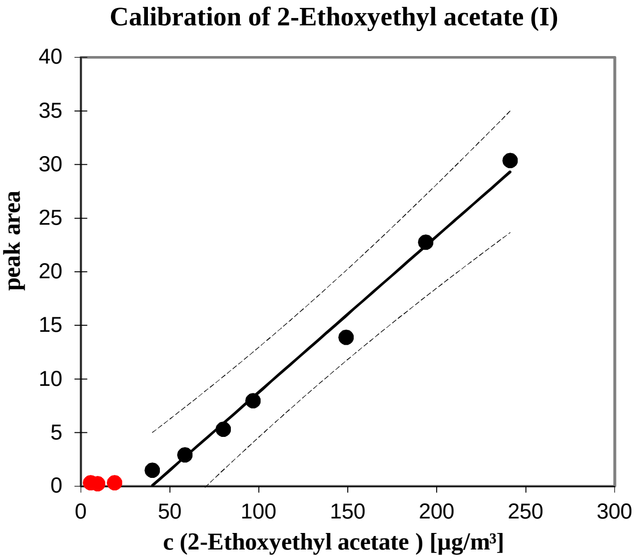


Figure 27: Calibration data of 2-Ethoxyethyl acetate with limited working range. [72]

To ensure the calculated limit of quantification from the 10-point-calibration, an additional calibration with six equidistant calibration points was carried out in a triple measurement for each approach. The results of the 6-point calibration are given in Appendix 3. The calibration range covers an order of magnitude and is based on the initial calculation of the quantification limit from the 10-Point-Calibration. For most analytes, the calculated quantification limit is below 10 µg/m^3 (Appendix 2). For validation, the concentration range for this calibration is therefore 2.5 to 25 µg/m^3.

An exception is 2-ethoxyethyl acetate, which cannot be determined in the intended measuring range. For this analyte, a high limit of quantification of 84 µg/m^3 was calculated from the 10-point calibration (Figure 27). The calibration range for 2-ethoxyethyl acetate for the additional calibration with six equidistant calibration points was set at 20 to 200 µg/m^3.

2-Ethoxyethyl acetate (II)

91 - 196 µg/m³

4 Calibration levels (n=3)

→ LOD considered

y = 0.121x – 7.657

r = 0.9994

V_{x0} = 1.34 %

LOD = 86 µg/m³

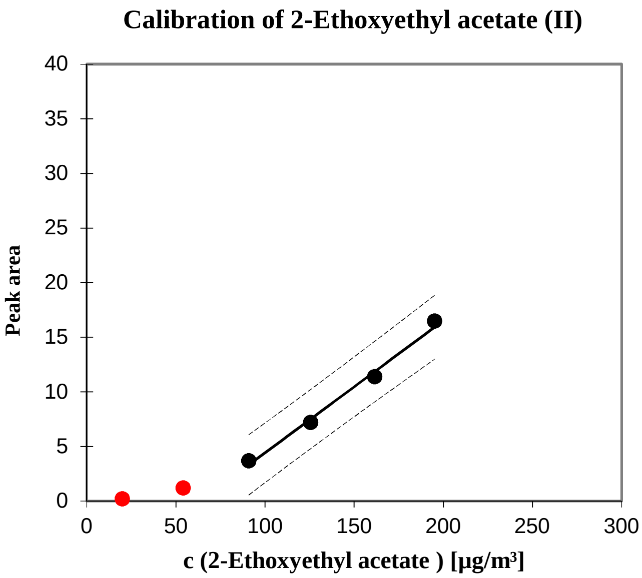


Figure 28: Second calibration of 2-Ethoxyethyl acetate to ensure the limit of quantification. [72]

The working range for 2-ethoxyethanol also has to be narrowed down owing to the calculation of the limit of quantification from the additional calibration, which is 15 µg/m³. Therefore, the lower calibration levels 5 and 10 µg/m³ are no longer quantifiable, so that only eight levels were evaluated instead of ten (Figure 29). In addition, the working range for 2-methoxyethanol, 1-methoxy-2-propanol and 1-ethoxy-2-propanol are limited. Because the limit of quantification lies above the first calibration level of the 10-point-calibration, the working range is limited to 10-250 µg/m³.

2-Ethoxyethanol

19 - 243 µg/m³

8 calibration levels (n=3)

y = 0.361x + 3.376

r = 0.9973

V_{x0} = 5.61 %

LOQ = 15 µg/m³

→ red calibration points < LOD

(restricted working range)

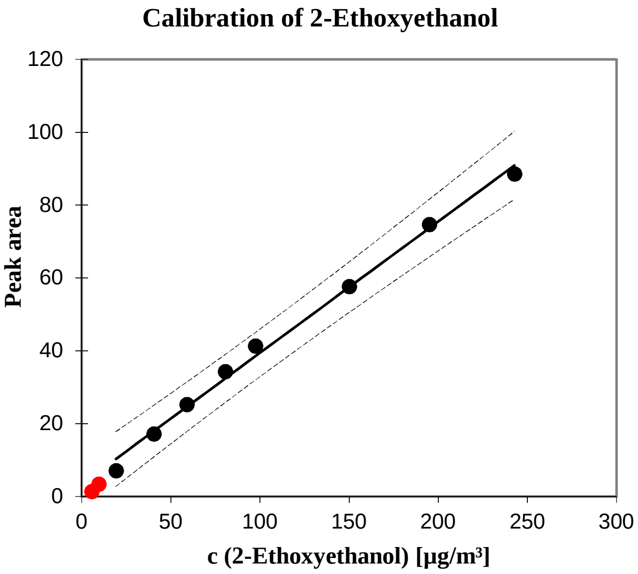


Figure 29: Calibration data of 2-Ethoxyethanol with limited working range. [72]

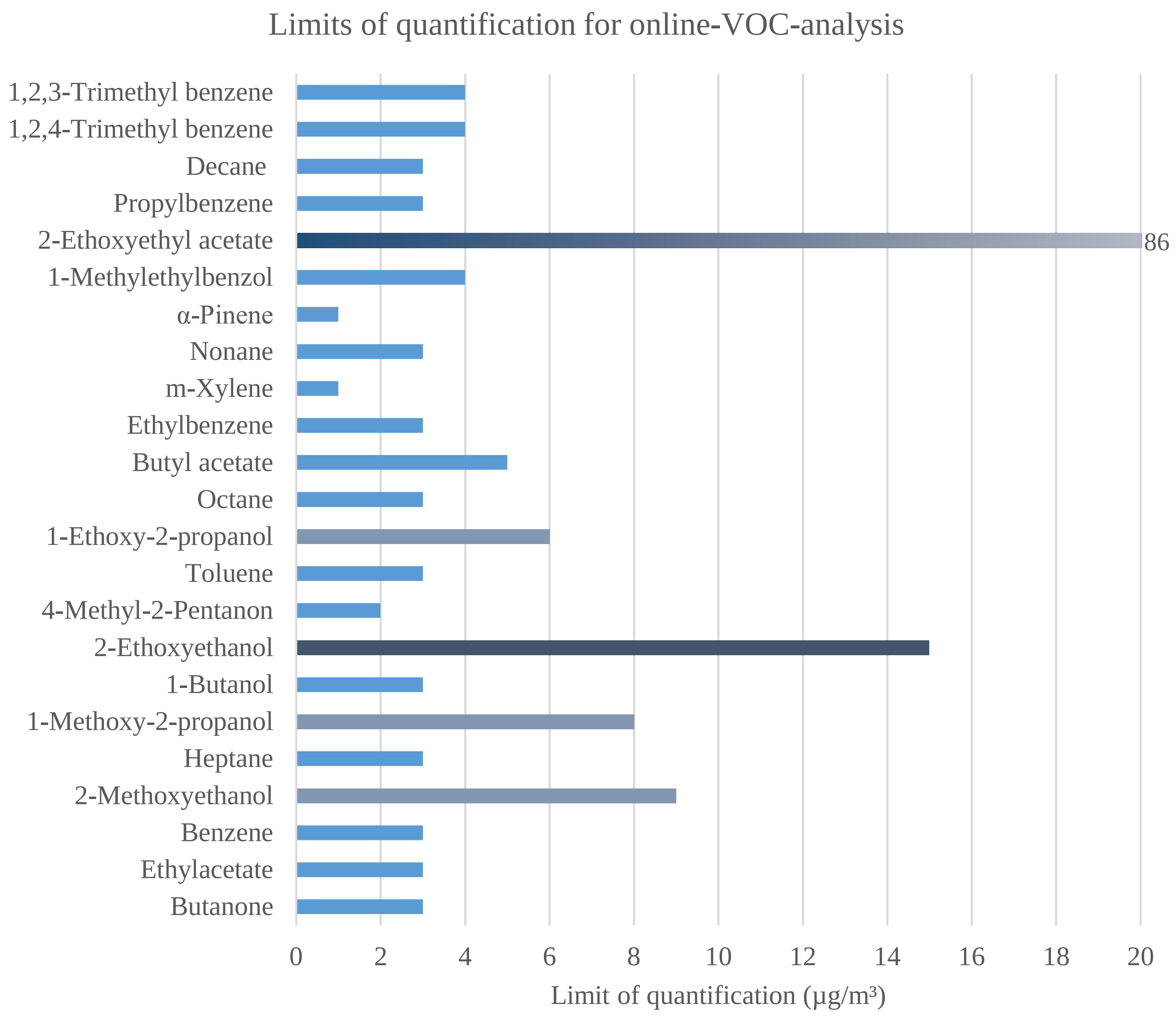


Figure 30: Limits of quantification. Determined by calibration line method from 6-point calibration. [72]

Tailing is pronounced at certain peaks. These include the glycol ethers 2-methoxyethanol, 1-methoxy-2-propanol, 2-ethoxyethanol and 1-ethoxy-2-propanol but not the glycol ester 2-ethoxyethyl acetate. The reason for tailing is an interaction of the polar groups with the active sites of the capillary column, such as the silanol groups on the capillary wall [80]. The additional retention increases the residence time of the analyte in the capillary. The phenomenon of asymmetric peaks is typical for the analysis of polar compounds on a (relatively) non-polar column. Most of the active sites have already been deactivated by the manufacturer to avoid interactions and also, the stationary phase acts as a shield depending on the layer thickness, so that only a fraction of the polar VOCs can interact with the active silanol groups [81]. Due to the tailing, a reproducible, complete integration of the uneven peaks can prove difficult, which is reflected in higher limits of quantification, see Figure 30.

5.1.4 Verification of the online-measurements with independent offline-TD-GC-MS analysis

In order to verify the results of the online control with regard to accuracy, offline measurements are carried out in parallel to the online measurement of a test gas using conventional, validated TD-GC-MS methods. Samples from the test gas facility are collected on Tenax® TA sample carriers. The concentrations of the multiple measurements were averaged. The recoveries of the online and offline methods were then calculated, whereby the recovery was based on the calculated target concentration. The test gases for quality control contain all 23 VOCs in different concentrations, so that the online method could not reliably quantify the co-eluting VOCs. Nevertheless, the recovery rate was calculated for them as well. Since the 1-methylethylbenzene peak is superimposed by the 2-ethoxyethyl acetate, a combined recovery rate is calculated. Also for octane and 1-ethoxy-2-propanol a combined recovery rate is calculated.

The acceptance range of the online method was set between 90 and 110 % recovery, based on the deviations from the target concentration. The average, minimum and maximum recovery rates of the four quality control test gas samples are listed in Appendix 4. The table in Appendix 4 also indicates the average concentration of the approaches. The relative standard deviation refers to the dispersion of a triple determination at each approach. In this context, it describes the precision of the measurement procedure, but it is also affected by minimal fluctuations of the dosing unit. The relative standard deviation of a triple determination is a maximum of 8.0 % for 2-ethoxyethyl ethanol. If all four QC test gases are considered, the average relative standard deviations are between 1.1 and 5.3 %. It is shown that also the VOCs butanone (recovery rate from 93.5 to 99.8 %) and heptane (104.4 -108.6 %) have an acceptable recovery despite its co-elution with ethyl acetate, respectively 2-methoxyethanol. At the selected concentrations, the quantification of butanone and heptane is not critically influenced by the respective interfering compound. For the respective co-eluting compounds ethyl acetate and 2-methoxyethanol, on the other hand, the recovery with an average of 128.3 and 47.9 %, respectively, is not acceptable. Consequently, ethyl acetate cannot be determined next to butanone and 2-methoxyethanol cannot be determined next to heptane at the chosen concentrations. Nonane and m-xylene and can be successfully quantified side by side at a high m-xylene (162.4 µg/m³) and a low nonane concentration (13.7 µg/m³) as shown in the recovery rates of 95.0 to 105.5 %. The recovery of 2-ethoxyethanol is particularly high with an average of 119.2 %. As discussed earlier, calibration is a limiting case of linearity, so that a high error load can occur for accuracy of the quantification. Except for the results of ethyl acetate, 2-methoxyethanol and 2-ethoxyethanol, the smallest recovery is 93.5 % for butanone and the largest 108.6 % for heptane. Thus, the recovery rates match with the previously defined acceptance range of 90 - 110 %.

The obtained recovery rates by the offline method are also largely within this range and confirm the definition of the acceptance limits. Exceptions are 2-methoxyethanol, nonane, 2-ethoxyethyl acetate and 1,2,3-trimethylbenzene. The determined recovery rate of 2-ethoxyethyl acetate is also critical with an average of 110.6 µg/m³. 2-ethoxyethylacetate was already conspicuous in previous measurements (see

Sections 5.2 and 5.3). The recovery rate of 2-methoxyethanol and 1,2,3-trimethylbenzene are outside the acceptance range at individual doses of the quality control test gas approaches, but not on average.

5.1.5 Influence of sample humidity on the online method

The evaluation here is also based on the calculation of recovery rates. In addition, the magnitude of homogeneous variances is evaluated by comparing two mean values using the t-test. Starting from 40 % relative humidity, the effect of dry air (20 % relative humidity) and moist air (60 and 80 % relative humidity) on the recovery rate was therefore investigated using the t-test. Furthermore, an outlier test according to Grubbs ($\alpha = 0.01$) was carried out and the variance homogeneity ($\alpha = 0.01$) was checked as a prerequisite for the t-test.

If the recovery rates at 40 % relative humidity are compared with moderate changes in humidity of ± 20 %, the t-test finds deviations in the recovery rate only for glycol ethers (see Figure 31 and Table 11). A reduction in relative humidity from 40 to 20 % causes a change in recovery only for 2-ethoxyethanol and 2-ethoxyethyl ethyl acetate. In contrast, a moderate increase in relative humidity from 40 to 60 % has an effect on the recovery rate of 2-methoxyethyl ethanol, 1-methoxy-2-propanol and 1-ethoxy-2-propanol. Sanchez and Sacks observed a similar effect of humidity on the thermal desorption-based analysis of the alcohols methanol, ethanol, 2- and 1-propanol. At 100 % relative humidity, the recovery decreased by 4 - 11 %, depending on the polarity of the VOCs. With alkanes as representatives of the non-polar VOCs, however, the recovery remained stable. [73] With a partition coefficient of log (-0.77) between octane and water, 2-methoxyethanol is the analyte of strongest polarity used in terms of this thesis and, accordingly, shows the strongest effect when humidity is increased. Sanchez and Sacks assume that the alcohols form hydrophilic dipoles with the water molecules, which cannot be adsorbed by a carbon-based cold trap. Accordingly, the recovery of non-polar VOCs is not affected by air humidity. The reduced recovery rate at low humidity, as observed with 2-ethoxyethylethanol and 2-ethoxyethylacetate, cannot be explained by this and is rather due to an error-prone quantification (see Appendix 2). While for 2-methoxyethanol a change in air humidity has a great influence on the recoveries, it is comparatively low for the remaining substances. Despite the effect of the air humidity proven by the t-test, only 2-methoxyethanol, 1-methoxy-2-propanol and ethyl acetate fell below the lower acceptance limit of 90 % recovery. A critical effect of the air humidity has been therefore only detected for the glycol ethers and esters and, to a lesser extent, for ethyl acetate (Appendix 5).

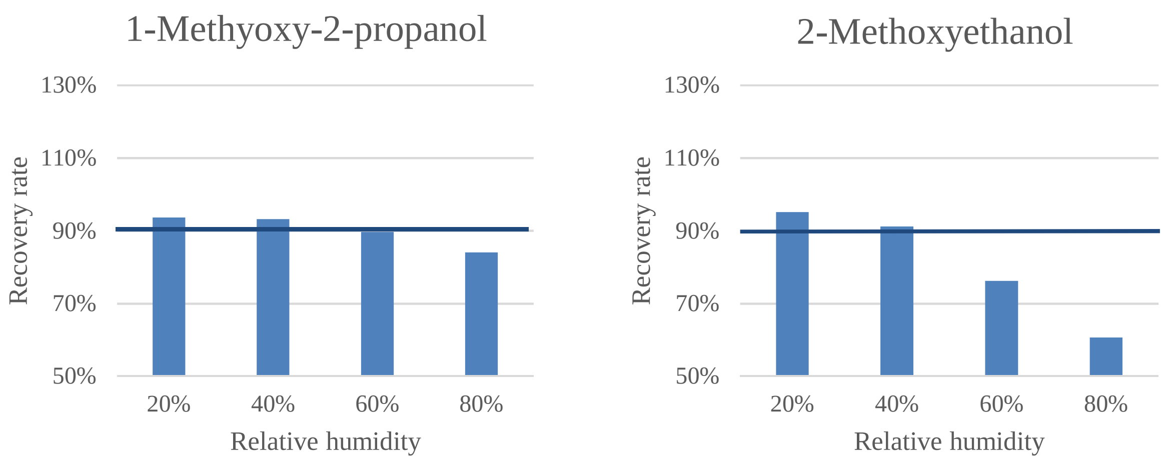


Figure 31: Influence of relative humidity on the recovery rates of 2-methoxyethanol and 2-methoxy-2-propanol. [72]

Table 11: Results of the extended t-test: with $t_{4;0.05} = 2.776$; effect of relative humidity RH at a: moderate reduction (from 40 to 20 %), b: moderate increase (from 40 to 60 %), c: strong increase (from 40 to 80 %) of the relative humidity. [72]

Analyte	Change in relative humidity [%]		
	a **40 to 20**	**b** **40 to 60**	**c** **40 to 80**
Ethyl acetate	no	no	yes
Benzene	no	no	yes
2-Methoxyethanol	no	yes	yes
1-Methoxy-2-propanol	no	yes	yes
1-Butanol	no	no	yes
2-Ethoxyethanol	yes	no	yes
4-Methyl-2-pentanone	no	no	no
1-Ethoxy-2-propanol	no	yes	yes
Butyl acetate	no	no	no
Ethylbenzene	no	no	yes
m-Xylene	no	no	yes
α-Pinene	no	no	yes
2-Ethoxyethyl acetate	yes	no	yes
Propylbenzene	no	no	no
Decane	no	no	no
1,2,4-Trimethylbenzene	no	no	no
1,2,3-Trimethylbenzene	no	no	no

5.1.6 Verification of the online VOC analysis during proficiency test

To verify the developed method for online control of VOC test gases, the method was used during the proficiency test. The test gas generated for the proficiency test contained nine compounds:

- 1,2,4-Trimethylbenzene
- α-Pinene
- Benzene
- Cumene
- Ethyl acetate
- Ethylbenzene
- Octane
- p-Xylene
- Toluene

The selection of substances for the proficiency tests is based on several criteria. The demand of the participants for substances that are important for their field is taken into account, as well as ensuring that the substances do not cause problems in the analytical procedure. Attention is also paid to the diversity of the substance classes. In addition to the substance characteristics, the analyte selection also takes into account that no co-elutions occur during online analysis, see Figure 32.

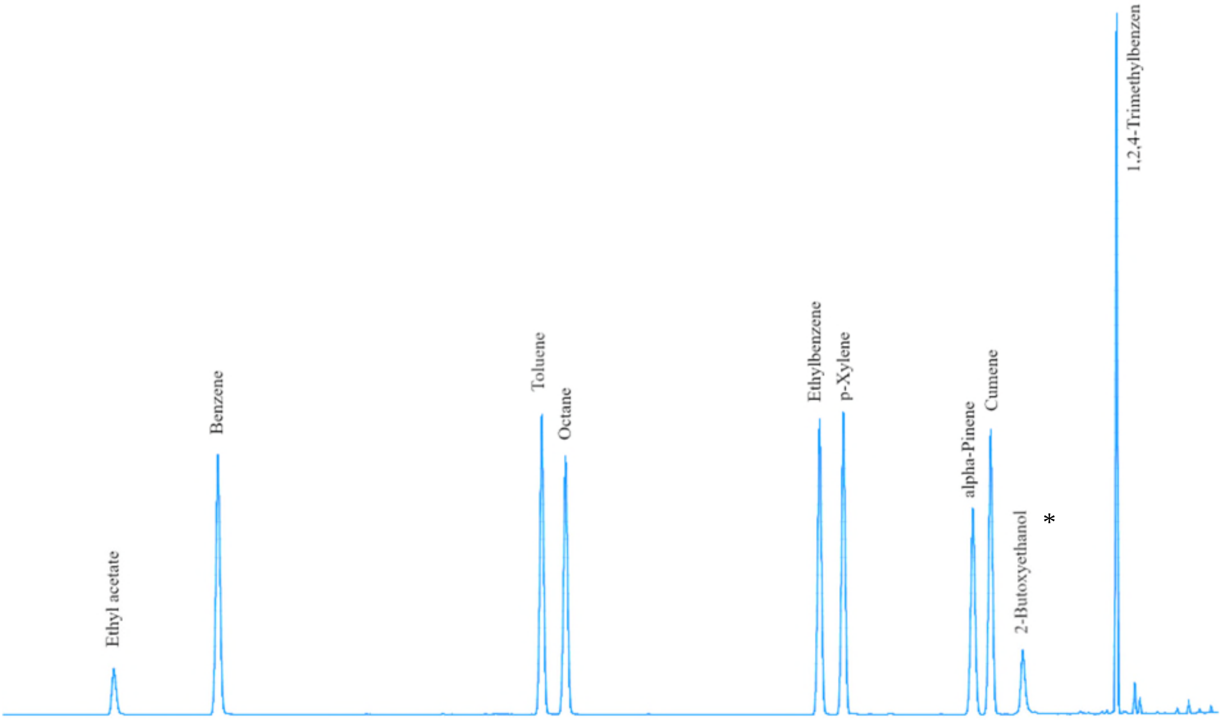


Figure 32: Substance selection for the 2019 VOC proficiency test. x-axis time in minutes, y-axis response in pA. * 2-Butoxyethanol is not chosen for the Proficiency test in 2019, the test gas only contains 2-Butoxyethanol for internal testing purposes.

For the proficiency test, two test gases with different concentrations of the selected analytes are prepared. The following diagrams (Figure 33 and Figure 34) show the recovery rates of the online analysis compared to conventional offline-GC analysis during the proficiency testing with on-site sampling for quality control purposes.

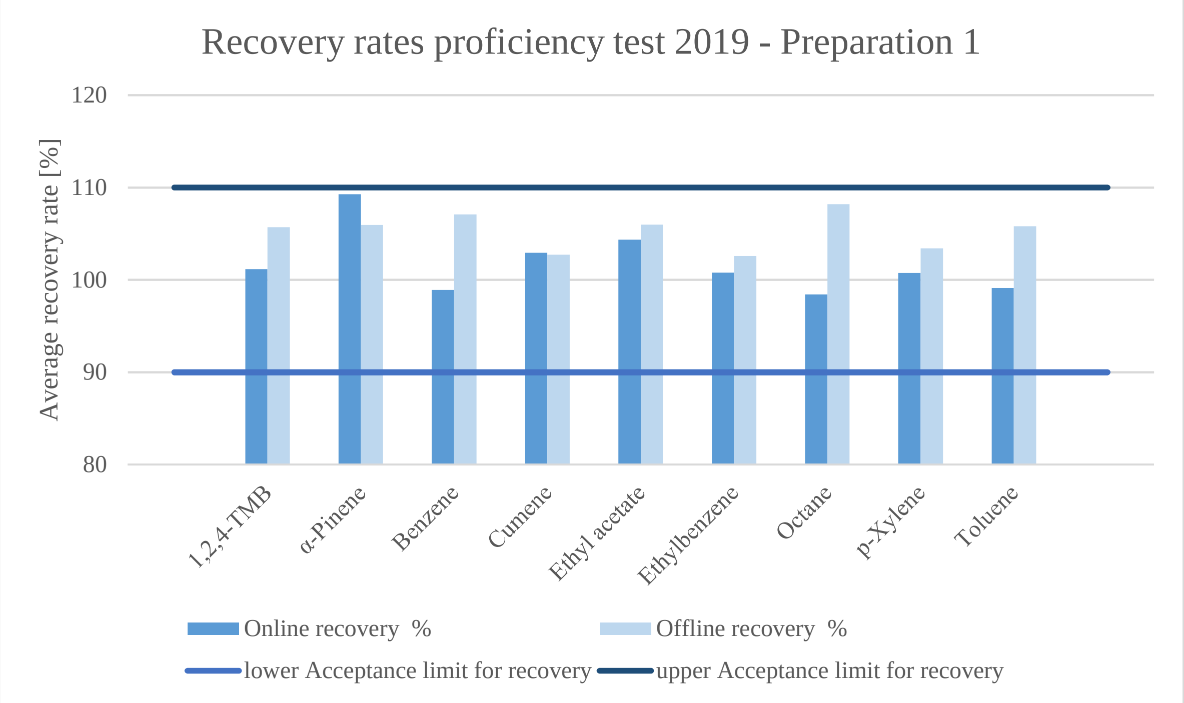


Figure 33: Average recovery rates of VOC's during the proficiency test for run 1. Determined by online and offline-GC measurements.

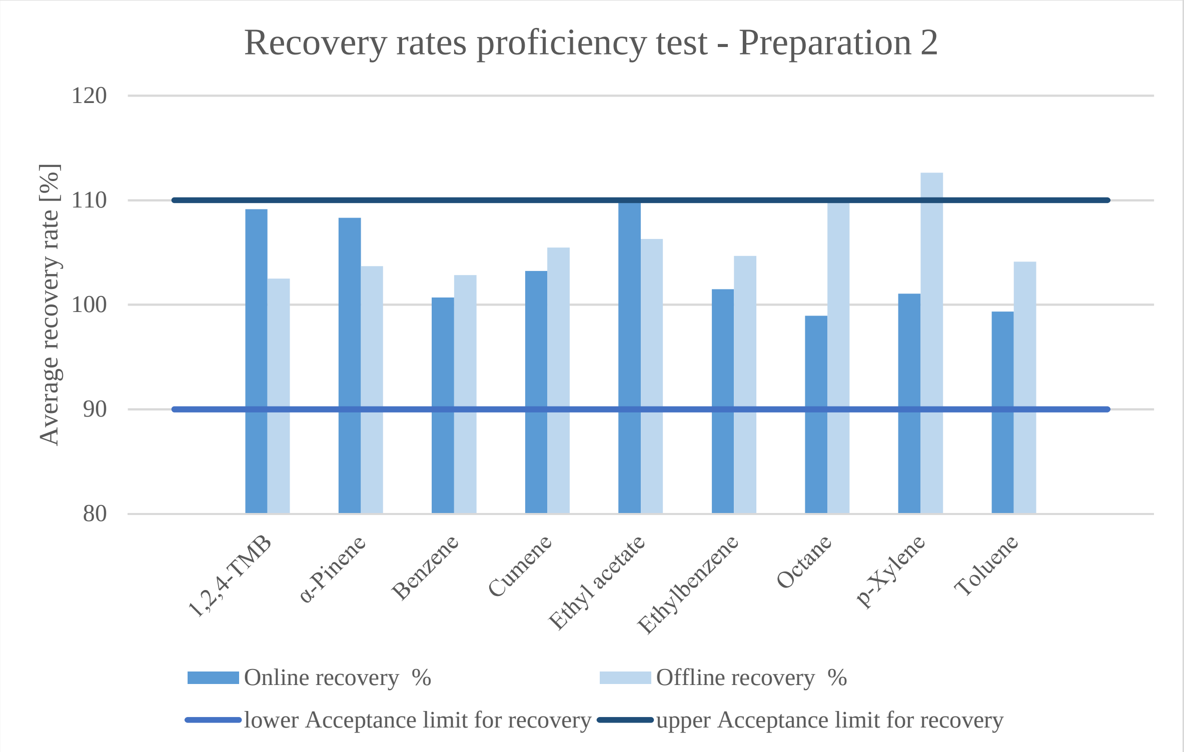


Figure 34: Average recovery rates of VOC's during the proficiency test for run 2. Determined by online and offline-GC measurements.

5.2 Results of the method development for the online determination of organic solvents

In this chapter, the results for the online control of organic solvents are presented. In addition to the results of the method development, the results of two proficiency tests are shown.

5.2.1 Retention time determination

For the online determination of organic solvents, the retention times of 33 compounds were identified see Table 12. The elution order is illustrated in Figure 35.

Table 12: Identified compounds for the organic solvent online method and their retention time.

Peak number	Organic solvent compound	Retention time [min]
1	n-Pentane	1.299
2	n-Hexane	1.330
3	n-Heptane	1.414
4	Cyclohexane	1.445
5	Methylcyclohexane	1.530
6	n-Octane	1.595
7	Acetone	1.635
8	Ethyl acetate	1.892
9	2-Butanone	1.943
10	Methanol	1.961
11	2-Methyl-2-Propanol	1.989
12	2-Propanol	2.128
13	Ethanol	2.147
14	Benzene	2.167
15	n-Decane	2.562
16	4-Methyl-2-Pentanone	2.583
17	i-Butyl acetate	2.640
18	2-Butanol	2.775
19	Toluene	2.821
20	1-Propanol	2.882
21	n-Butyl acetate	3.132
22	2-Methyl-1-Propanol	3.340
23	Ethylbenzene	3.600
24	1-Methoxy-2-Propanol	3.668
25	p-Xylene	3.670
26	m-Xylene	3.736
27	1-Butanol	3.860
28	Cumene	4.073
29	Cyclopentanone	4.183
30	1-Methoxy-2-propylacetate	4.647
31	1,2,4-Trimethylbenzene	5.028
32	2-Ethoxyethylacetate	5.125
33	2-Butoxyethanol	5.567

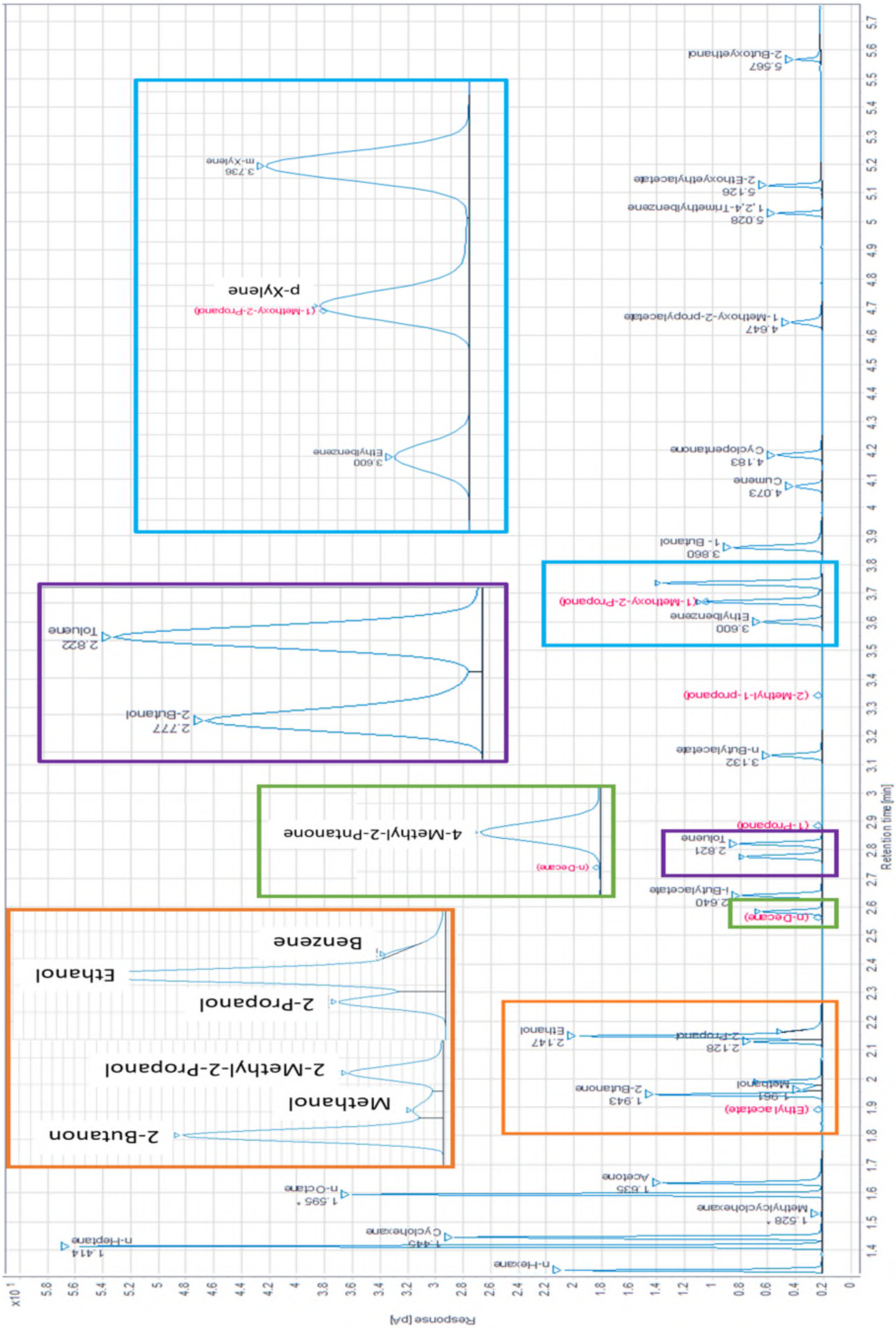


Figure 35: Chromatogram of the method for online organic solvents analytics. (The substances written in red were not available during method development and were added later).

5.2.2 Determination of the method parameters

As described previously, the separation takes place on the Zebron ZB-WAXplus column. The method parameters for the best possible separation with the shortest analysis time are summarized in the following (Table 13 and Table 14).

Table 13: Oven program for organic solvent online analysis.

	Rate [°C/min]	Value [°C]	Hold time [min]	Run time [min]
Initial		30	0.5	0.5
Ramp 1	12	80	0	4.66
Ramp 2	max	200	0	5.76

Table 14: Flow parameters for organic solvent online analysis.

Flow [mL/min]	1.9494
Average velocity [cm/s]	55
Split ratio	50:1
Split flow [mL/min]	97.47

Compared to the online-method for the analysis of VOCs, the analysis time was much faster because of the absence of preconcentration. The analysis time here was 5.7 minutes.

5.2.3 Calibration

After successful development of the measurement method, calibration was performed according to the selection of the analytes used in the proficiency test. In contrast to the VOC proficiency test, three test gas mixtures with different analytes have been provided during the proficiency test for organic solvents. Another difference is that the concentration range for the dosed analytes depends on their individual occupational exposure limit and there is no fixed concentration range for all analytes. The basic requirement for the concentration range during a proficiency test for each individual analyte is between 0.01- and 2-times of its occupational exposure limit.

Although the analytes are contained in three independent test gases, the calibration is nevertheless performed in one approach for all analytes of the proficiency test. Since the development of the method, the method has been used in two proficiency tests. The calibration results and results of the proficiency test are presented in the following sections.

5.2.3.1 Calibration for proficiency test 2018

The following (Table 15) shows the analytes used in the 2018 proficiency test with their respective occupational exposure limit values, the planned concentration during the proficiency test and the calibration range.

Table 15: Proficiency testing 2018 (PT 2018) for organic solvents: Analyte selection with their occupational exposure limits [12], concentration and calibration range.

Compound	Occupational Exposure Limit **[mg/m³]**	Concentration PT 2018 [mg/m³]	Calibration range [mg/m³]
n-Decane	250	35.7	7.1 – 71.1
Cumene	50	15.3	3.1 – 30.6
p-Xylene	440	102	20.3 – 203
Ethylbenzene	88	35.2	7.0 – 70.3
n-Octane	2400	264	52.2 – 522
1-Butanol	310	62.6	12.6 – 126
Toluene	190	61.1	12.1 – 121
2-Methyl-1-Propanol	310	115	22.8 – 228
Methyl cyclohexane	810	57.0	11.5 – 115
2-Butanol	305	80.8	16.6 – 166
n-Heptane	2100	301	59.0 – 590
1-Propanol	500	397	78.8 – 787
Cyclohexane	700	62.8	14.0 – 140
Ethyl acetate	1500	255	50.7 – 507
n-Hexane	180	28.0	5.90 – 58.8

The broad range between 0.01- and 2-times of the occupational exposure limit and the widely spreading OELs of the individual substances are hardly to be realized with the setup of the dosing unit (HovaCal). It has been decided to adapt the calibration to the defined concentration in the proficiency test. The five-point calibration is set up in a way that the concentration for the proficiency test lies in the middle of the calibration range.

The preparation of the dosing solution for the calibration depends on the percentage of the respective analyte in the proficiency test in relation to the total concentration. Thus, the sometimes considerably different concentrations of the substances for calibration can be realized with one dosing solution.

The following diagram (Figure 36) gives an overview of the calibrations of the individual analytes of the proficiency test.

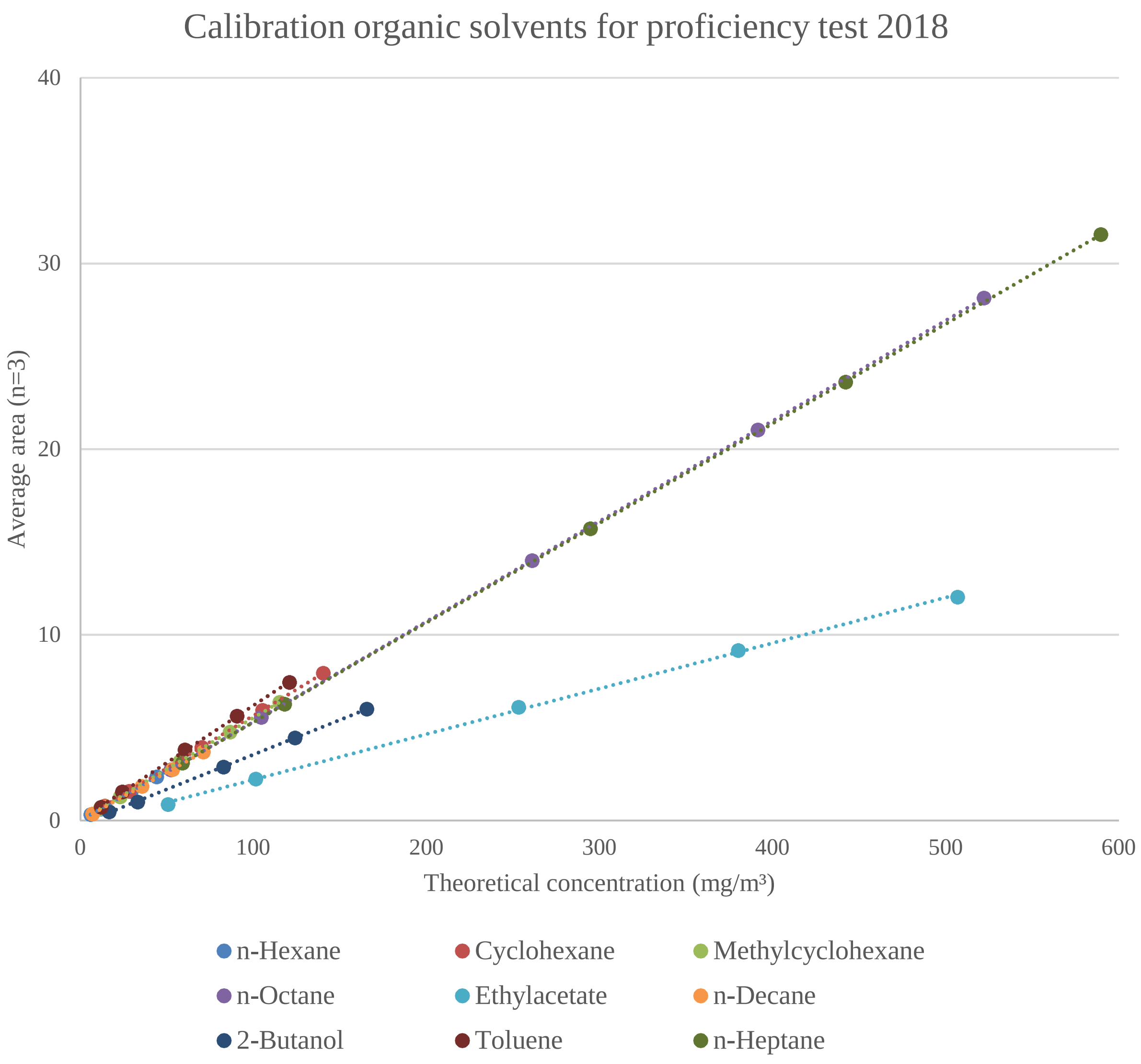


Figure 36: Calibration of organic solvents in the mg/m³ range for the proficiency test 2018.

All correlation coefficients were between 0.9996 and 1. The limit of quantification calculated from this calibration varies from 0.824 mg/m³ for n-hexane to 58.8 mg/m³ for ethyl acetate. Due to the different calibration range of the individual substances, the limit of quantification should, however, be assessed with regard to the calibration range and the defined concentration during the proficiency test. Therefore, the defined concentration, the lowest calibration level and the analytical limits obtained from calibration are summarized in Table 16. A detailed summary of the calibration can be found in the Appendix 6. The evaluation of the calibration is carried out according to DIN 32645. [77]

Table 16: Analytical limits of the calibration for organic solvents proficiency test 2018 (PT 2018).

Compound	Concentration PT 2018 [mg/m³]	Calibration range [mg/m³]	Correlation coefficient r	Limit of quantification [mg/m³]
n-Hexane	28.0	5.89 – 58.8	1.0000	0.82
n-Heptane	301	59.0 – 590	1.0000	3.06
Cyclohexane	62.8	14.0 – 140	0.9999	1.01
Methyl cyclohexane	57.0	11.5 – 115	0.9999	1.07

Compound	Concentration PT 2018 [mg/m³]	Calibration range [mg/m³]	Correlation coefficient r	Limit of quantification [mg/m³]
n-Octane	264	52.2 – 522	1.0000	4.21
Ethyl acetate	255	50.7 – 507	0.9996	58.8
n-Decane	35.7	7.11 – 71.1	1.0000	1.36
2-Butanol	80.8	16.6 – 165	0.9999	9.72
Toluene	61.1	12.1 – 121	0.9999	8.22
1-Propanol	397	78.8 – 787	0.9999	37.6
2-Methyl-1-propanol	115	22.8 – 228	1.0000	3.97
Ethylbenzene	35.2	7.03 – 70.3	1.0000	0.92
p-Xylene	102	20.3 – 203	1.0000	3.41
1-Butanol	62.6	12.6 – 126	0.9997	12.8
Cumene	15.3	3.07 – 30.6	0.9999	1.48

The limit of quantification is below the lowest calibration point for almost all substances. Only for ethyl acetate the limit of quantification of 58.8 mg/m³ is significantly above the first calibration point (50.7 mg/m³). With regard to the correlation coefficient, this can also most likely to be expected for ethyl acetate. The limit of determination for 1-butanol with 12.8 mg/m³ is only slightly above the lowest calibration level of 12.6 mg/m³. Nevertheless, the LOQ is far below the concentration of the respective substance during the proficiency test (ethyl acetate 255 mg/m³, 1-butanol 62.6 mg/m³). The reason for the relatively poor calibration result of ethyl acetate is the peak shape. Ethyl acetate shows a clear tailing in the chromatogram, which makes a reproducible quantification difficult.

For the quality control samples, three concentrations are set and measured along the calibration range with a separately prepared test gas. The recovery rates are shown in the following diagram (Figure 37); the complete evaluation is given in Appendix 7.

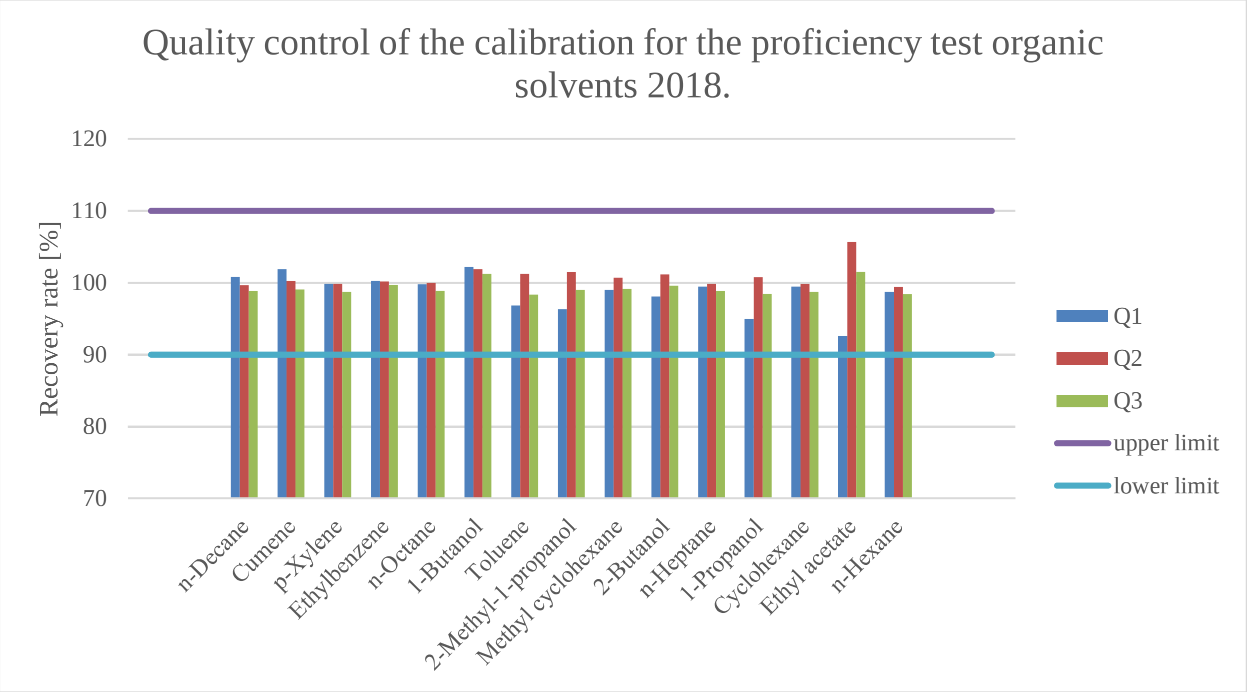


Figure 37: Quality control of the calibration for the proficiency test organic solvents 2018.

As can be seen in the figure above, all analytes of the quality control samples are within the previously mentioned defined limits of ±10%. As in the calibration, ethyl acetate is conspicuous here, but is within the set limits.

5.2.3.2 Calibration for proficiency test 2019

Calibration for the 2019 proficiency test is carried out in the same way as for the calibration in 2018. Table 17 shows a summary of the most important results. A more detailed summary is given in Appendix 8.

Table 17: Calibration summary Proficiency test 2019 for organic solvents in the mg/m³ range, including analytical limits.

Compound	Concentration PT 2019 [mg/m³]	Calibration range [mg/m³]	Correlation coefficient r	Limit of quantification [mg/m³]
n-Decane	66.3	5.55 – 118	1.0000	0.70
Cumene	9.49	0.86 – 18.3	1.0000	0.43
m-Xylene	62.2	5.45 – 116	1.0000	1.07
Methylcyclohexane	105	9.76 – 207	1.0000	2.09
2-Butanol	32.9	2.98 – 63.3	0.9965	17.7
1-Propanol	143	12.6 – 268	0.9990	43.7
2-Propanol	116	10.4 – 221	0.9984	44.4
Cyclohexane	114	10.2 – 217	1.0000	3.45
Ethyl acetate	186	16.8 – 358	0.9964	101
1,2,4-Trimethyl benzene	93.5	8.55 – 182	0.9996	19.7
n-Nonane	249	16.9 – 360	1.0000	5.18
Ethylbenzene	67.4	6.04 – 128	1.0000	2.34
1-Butanol	69.9	6.54 – 139	0.9992	20.7
Toluene	44.9	3.79 – 80.6	1.0000	0.90
2-Methyl-1-Propanol	92.5	8.30 – 176	0.9990	28.6
Ethanol	253	22.6 – 480	0.9994	60.9
n-Hexane	21.7	1.88 – 40.0	1.0000	0.78

Compared to the calibration from the previous year, it is noticeable here that some analytes have a somewhat smaller correlation coefficient than in the previous year. Apart from ethyl acetate, it is noticeable that all alcohols show somewhat poorer correlation coefficients relative to the non-polar components. The effect is also transferred to the quality control samples. This may possibly be attributed to potential aging of the separation column. The already mentioned substances also show poor correlations regarding the recovery rate, whereas all other substances are in the range between 90 and 110 % recovery, see Figure 38.

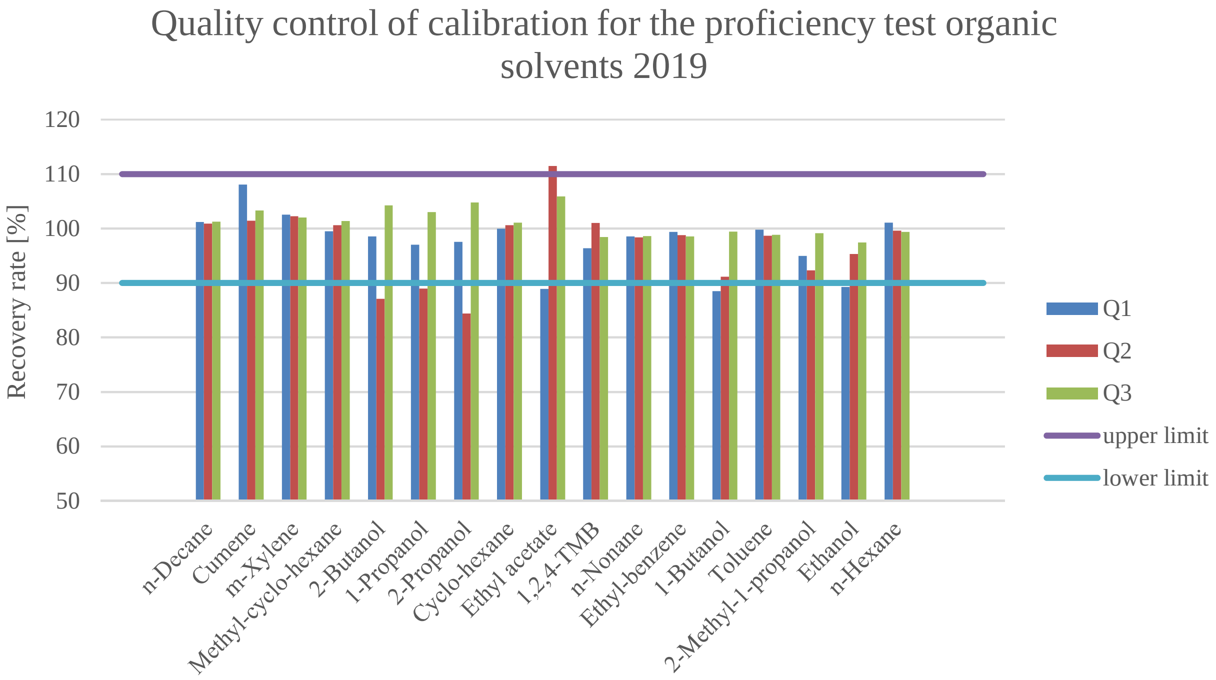


Figure 38: Quality control of calibration for the proficiency test organic solvents 2019.

5.2.4 Results of the online control of organic solvents during the proficiency tests 2018 and 2019

After calibration, the method is used during the proficiency test. In addition to the online control, internal quality measurements of sample carriers are performed with a validated offline-GC method. The results are presented below as examples for the 2018 and 2019 proficiency testing schemes. The complete evaluation of all experiments can be found in Appendix 9 to Appendix 11.

5.2.4.1 Results of the online measurements during the proficiency testing scheme 2018

An example of the continuous monitoring behavior during proficiency testing is shown in the following table (Table 18) and the corresponding graphical representation (Figure 39) for test gas mixture one.

Table 18: Results of test gas mixture 1 of proficiency test for organic solvents 2018. Comparison online and offline measurements.

Test gas mixture 1	Calculated conc. [mg/m^3]	Method	Min. concentration [mg/m^3]	Max. concentration [mg/m^3]	Average concentration [mg/m^3]	Standard deviation [mg/m^3]	Relative standard deviation [%]	Recovery rate [%]
Cyclohexane	62.5	Online-GC (n=25)	63.0	65.9	64.8	0.78	1.2	104
		Offline-GC (n=10)	62.1	64.4	63.1	0.68	1.1	101
n-Decane	35.5	Online-GC (n=25)	35.0	36.9	35.9	0.43	1.2	101
		Offline-GC (n=10)	34.8	36.3	35.4	0.41	1.2	100
n-Heptane	300	Online-GC (n=25)	298	311	305	3.7	1.2	102
		Offline-GC (n=10)	308	319	312	3.3	1.1	104
n-Hexane	27.8	Online-GC (n=25)	27.8	29.6	28.7	0.47	1.6	103
		Offline-GC (n=10)	30.4	31.4	30.8	0.31	1.0	111
Methyl cyclohexane	56.8	Online-GC (n=25)	56.2	59.6	58.1	0.88	1.5	102
		Offline-GC (n=10)	59.5	61.5	60.4	0.59	1.0	106
n-Octane	263	Online-GC (n=24)	260	273	267	3.5	1.3	102
		Offline-GC (n=10)	269	278	273	2.9	1.0	104

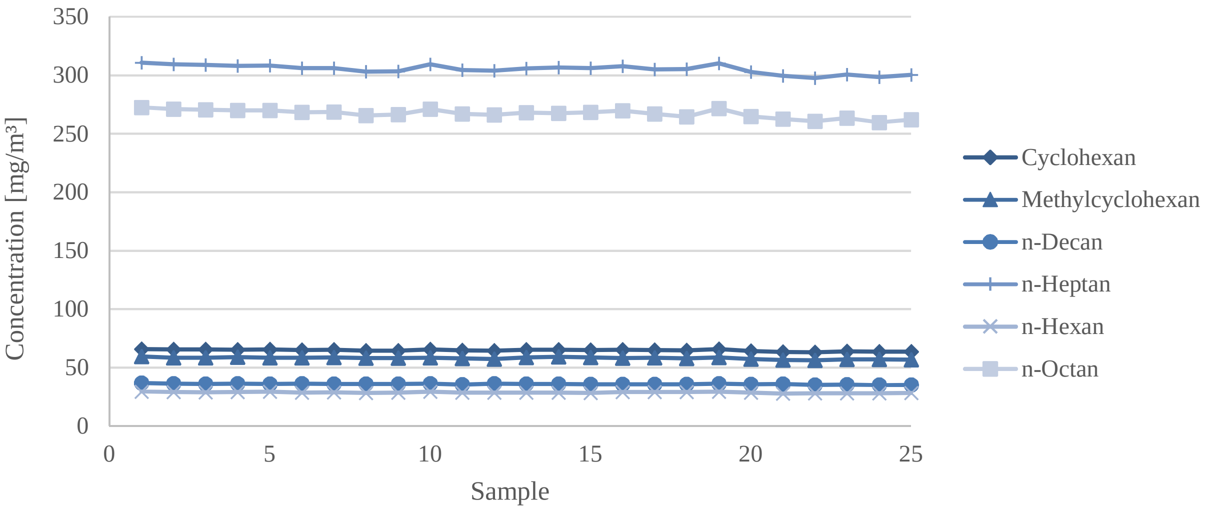


Figure 39: Monitoring of a test gas mixture during proficiency testing scheme 2018 for organic solvents with an online-GC method.

The figure above (Figure 39) clearly shows again that substances of low concentrations (<50 mg/m³) can be quantified stably in the presence of substances of high concentration (>300 mg/m³) over a longer period. Furthermore, the low relative standard deviation (1.2 - 1.6 %) of the online measurements over more than two hours proves the presence of a homogeneous test gas on the one hand and the precision of the measuring method on the other.

The indicator for correctness is the recovery. Both the recovery rate of the theoretically calculated concentration and the comparison with the results of the validated offline quality control confirm the correctness of the online measurement results within the tolerance of plus minus 10 %.

For the test gases two and three of the proficiency test, only the recovery rates of the online and offline control in relation to the theoretically calculated concentration value are shown below (Figure 40 and Figure 41). The result values are given in Appendix 10

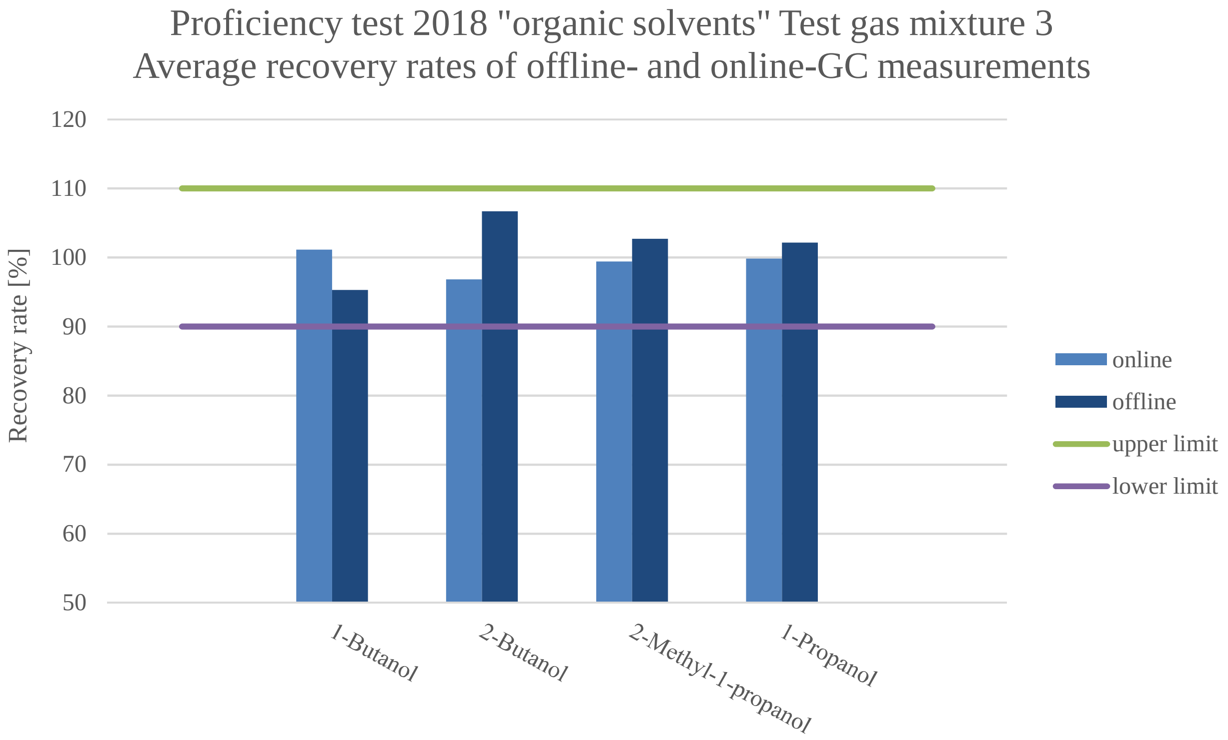


Figure 40: Proficiency test 2018 "organic solvents" test gas mixture 3. Average recovery rates for offline- and online-GC measurements.

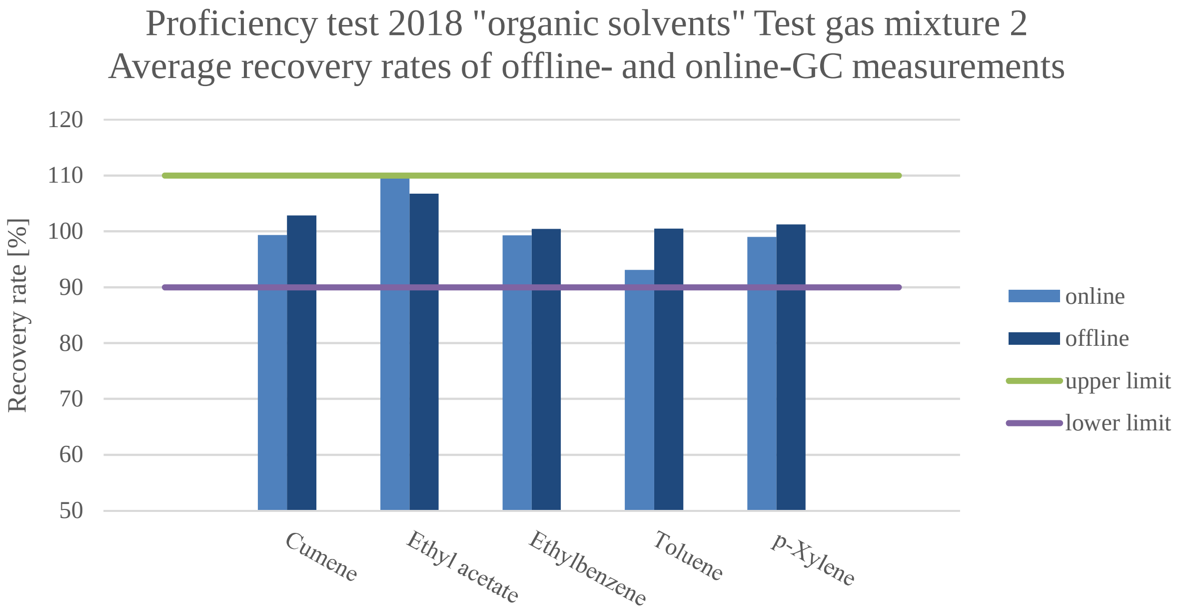


Figure 41: Proficiency test 2018 "organic solvents" test gas mixture 2. Average recovery rates for offline- and online-GC measurements.

5.2.4.2 Results of the online measurements during the proficiency testing scheme 2019

As the results of the calibration for the proficiency test organic solvents 2019 have suggested, the recovery is not within the tolerance range of 90-110 % for all substances. Ethyl acetate again proves to be problematic in terms of recovery. In 2018, however, the recovery was at the upper tolerance limit with 109.7 % (Figure 41), whereas during the proficiency test in 2019 it was well below the lower tolerance limit with 78.9 % (Figure 42). Comparing the calibrations with each other, the concentration value of the proficiency test 2018 with 253 mg/m³ is clearly above the limit of quantification of 59 mg/m³. For the 2019 calibration, a limit of determination of 100 mg/m³ is calculated and thus the proficiency test concentration of 186 mg/m³ is also significantly higher, but not by a multiple. Looking at the calibration, its range starts in 2019 with 16 mg/m³, which is significantly lower than in 2018 with 50 mg/m³. Since the peak shape changes with increasing concentration due to the greater influence of tailing, the linear range for quantification on this column seems to be limited.

Figure 42 shows the results of the recovery rates of the online and offline-GC measurements of the proficiency test of all three test gas mixtures. The individual results are provided in Appendix 11.

In addition to ethyl acetate, 2-propanol has also an insufficient recovery. With a recovery rate of 84.5 % it is below the 90 % tolerance limit. However, the other alcohols, some of which showed poor recovery in the calibration quality control samples, are within the 90-110 % tolerance in the proficiency test.

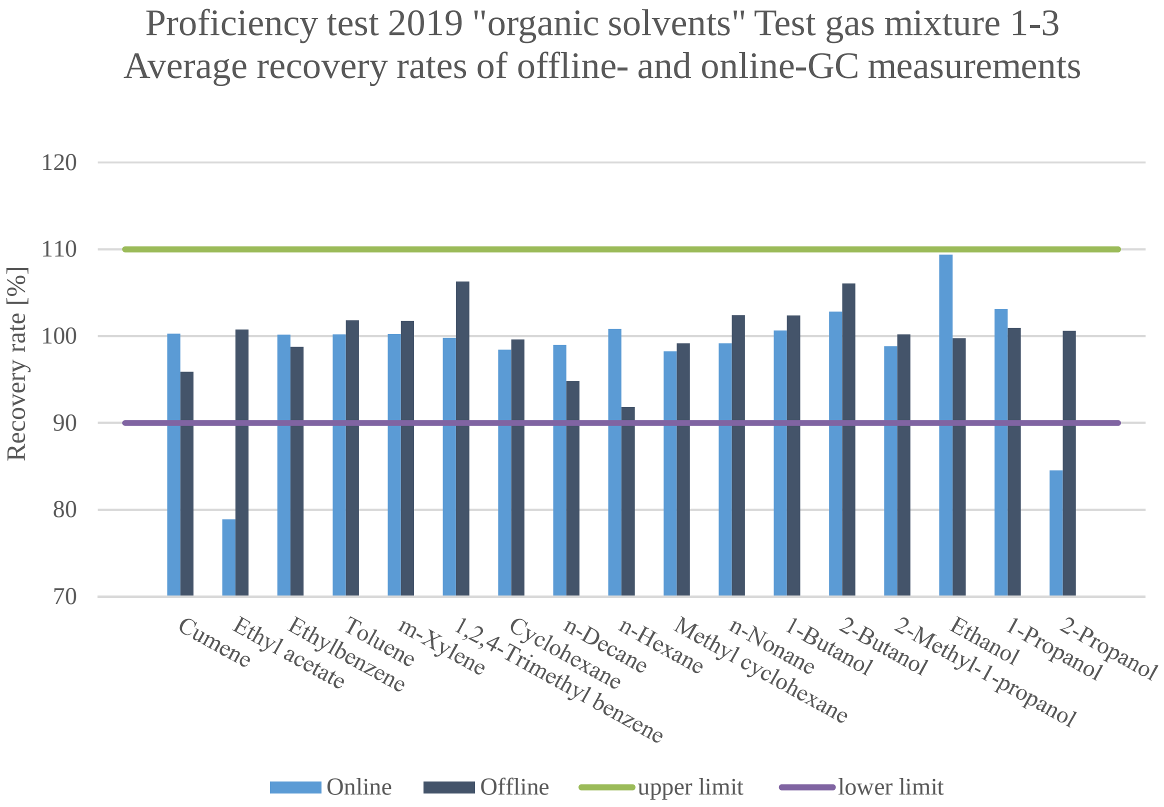


Figure 42: Results of the proficiency test 2019 for organic solvents (Summary of test gas mixtures 1-3): Average recovery rates of offline- and online-GC measurements.

5.3 Conclusion for the gas chromatographic measuring methods

In conclusion, it can be stated that the gas chromatographic measuring methods developed are suitable for online monitoring of solvent test gases in the mg/m³ range and VOC test gases in the µg/m³ range. With regard to the variety of substance classes used in the proficiency tests and the shortest possible analysis time required for online measurement methods, there are limitations that should be kept in mind. For example, the limited selectivity should be taken into account when selecting the substances for the respective proficiency test. Due to the short analysis time required for both online-GC measurement methods, selective quantification cannot be guaranteed over the entire substance range. When selecting substances for the proficiency test VOCs, the following substance combinations cannot be separated and should therefore be avoided:

- 1-Ethoxy-2-propanol and n-octane
- Cumene and 2-ethoxyethyl acetates
- m-Xylene and p-xylene

For the proficiency test of organic solvents, the combination of the following substances is not recommended to ensure a selective quantification:

- Ethanol and benzene
- p-Xylene and 1-methoxy-2-propanol

When comparing the recovery rates of conventional offline analysis of loaded sample carriers with the developed online methods, the online methods are equally suitable for quantification during a proficiency test.

5.4 Online determination of VOC test gas mixtures via SIFT-MS during proficiency test 2019

As the selection of the product ions used for quantification of the VOC real-time determination in the µg/m³ range is already described in 4.3.2.1, in this chapter only the results obtained during the proficiency test are shown.

The relevant calibration functions are shown in Appendix 12. The reaction rates calculated based on the calibration lines are shown in the Table 19.

Table 19: Calculated reaction rates of several VOCs from the test gas mixture used in 2019th proficiency test.

Compound	Reagent ion	Product	Reaction rate k from syft library [cm³ molecule^{-1} s^{-1}]	Reaction rate k calibrated within this work [cm³ molecule^{-1} s^{-1}]
α-Pinene	NO^+	$C_{10}H_{16}^+$ [136]	1.8E^{-09}	1.8E^{-09}
	H_3O^+	$C_{10}H_{17}^+$ [137]	1.5E^{-09}	1.4E^{-09}
Benzene	NO^+	$C_6H_6^+$ [78]	1.9E^{-09}	1.3E^{-09}
	O_2^+	$C_6H_6^+$ [78]	2.2E^{-09}	1.6E^{-09}
	H_3O^+	C_6H_6• H^+ [79]	2.4E^{-09}	1.6E^{-09}
Ethyl acetate	NO^+	NO^+•$CH_3COOC_2H_5$ [118]	2.6E^{-09}	2.4E^{-09}
Octane	O_2^+	$C_8H_{18}^+$ [114]	1.2E^{-09}	3.3E^{-10}
Sum 1,2,4-trimethylbenzene and Cumene	O_2^+	$C_8H_9^+$ [105]	1.1E^{-09}	7.0E^{-10}
	NO^+	$C_9H_{12}^+$ [120]	1.7E^{-09}	1.6E^{-09}
Sum Ethylbenzene and Xylene	O_2^+	$C_7H_7^+$ [91]	5.9E^{-10}	6.0E^{-10}
Toluene	NO^+	$C_7H_8^+$ [92]	2.4E^{-09}	1.8E^{-09}

As already mentioned, SIFT-MS analysis is an additional quantitative method to the online gas chromatographic analysis. The big advantage of SIFT-MS analysis compared to online GC analysis is its speed, which makes it possible to quantitatively determine the equilibration behavior (Figure 43) as well as the sampling period in real time (Table 20).

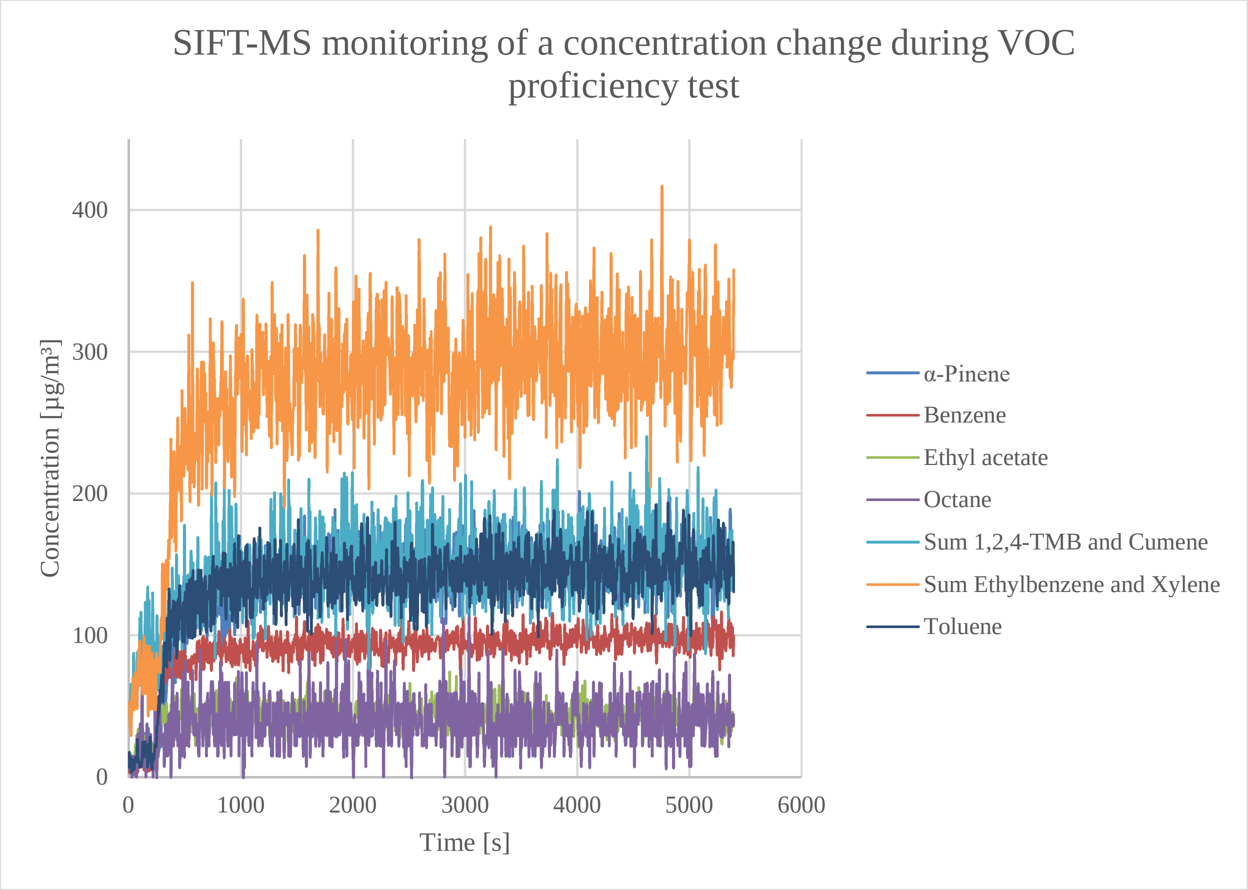


Figure 43: SIFT-MS monitoring concentration change during VOC proficiency test.

The data in the following Table 20 are collected over a period of approximately 40 minutes and include the sampling period for offline analysis.

Table 20: Monitoring behavior of SIFT-MS during the proficiency test

	Concentration [µg/m³]			Standard deviation [µg/m³]	Relative standard deviation [%]
	Min	Max	Average		
α-Pinene	118	147	134	7.0	5.2
Benzene	80.3	94.4	89.9	2.8	3.1
Ethyl acetate	34.4	39.0	36.1	1.2	3.3
n-Octane	27.6	39.9	33.4	3.9	12
Toluene	132	143	136	3.6	2.6

With the exception of octane, the analytes in the test gas can be analyzed with a relative standard deviation of <10% over the mentioned period. With a reaction rate of 3.3E^{-10} cm³ molecule^{-1} s^{-1} the reaction of octane with O_2^+ is a rather slow ion molecule reaction and also the sensitivity is low compared to the other substances with a slope of the calibration line of 0.27 (see Appendix 12).

Octane, with a recovery of 89%, is nevertheless within the target range of 80-120% recovery and all other analytes are found in this range. The only exception is the sum concentration of p-xylene and ethylbenzene with a total recovery of 140 %. The results are shown in comparison with the results of the gas chromatography in Table 21.

Table 21: SIFT-MS results obtained during proficiency test 2019.

	Benzene	Toluene	α-Pinene	Ethylacetate	Octane	p-Xylene	Ethylbenzene	Cumene	1,2,4-Trimethylbenze
Expected concentration [µg/m³]	83.5	118	129	36.9	37.5	49.7	141	43.3	85.2
Offline-GC result [µg/m³]	86.7	122	133	39.1	41.6	52.7	144	45.7	87.5
Online-GC result [µg/m³]	82.3	114	141	30.5	36.3	49.2	140	43.9	90.8
SIFT-MS result [µg/m³]	89.9	136	134	36.1	33.4	268		122	
SIFT-MS recovery rate [%]	**108**	**116**	**104**	**98**	**89**	**140**		**95**	

5.5 Method development for real time analysis of aldehyde test gases with SIFT-MS

For aldehyde test gases in the IFAs test gas facility, the analysis by means of SIFT-MS is the only specific online analysis currently in use. The SIFT-MS technique is used to test the newly developed dosing system for its planned use as a generator for aldehyde test gases. For this purpose, a measuring method analogous to the procedure in chapter 4.3.1 has been developed, which has then been validated in order to be able to make quantitative statements about the applicability of the dosing system as a test gas generator.

Since the SIFT-MS is a selective direct-reading analysis system, it is suitable for recording the behavior of the generated test gas in real time and, therefore, has been used to validate the newly developed dosing system. Even though the dosing system can be used universally, it is primarily intended to replace the dosing system used up to now (see 3.2.3) for generating aldehyde test gas. Consequently, the aim of this thesis is to conduct a feasibility analysis of the designed dosing system for the generation of aldehyde test gases from pure liquids for the proficiency test.

5.5.1 Checking the concentration of the test gases generated by the new dosing system by HPLC and simultaneous calibration of the SIFT-MS Method

In order to verify that the actual measured concentration of the generated test gas corresponds to the calculated concentration, a calibration series was set up. The change of the concentration is achieved by changing the split ratio. Since the SIFT-MS is not calibrated, the generated test gases are additionally analyzed by HPLC according to the IFA workbook. [70]

At the beginning of the method development, all non-interfering masses are selected to determine the aldehyde concentrations. This way, the reactions with their respective product ions best suited for quantification are determined in the second step. Table 22 shows a list of all available reagent ions, the corresponding reactions and the corresponding reaction rates and branching ratios.

Table 22: SIFT-MS: List of reactions for aldehyde analysis. [39]

Compound	Reagent ion	Reaction rate k [cm^3 molecule -1 s-1]	Branching ratio [%]	Mass (m/z)	Product	Scan	Calculated
Acetaldehyde	H_3O^+	$2.4E^{-9}$	100	45	$C_2H_5O^+$	✓	✓
	H_3O^+	$2.4E^{-9}$		63	$C_2H_5O^+ \cdot H_2O$	✓	✓
	H_3O^+	$2.4E^{-9}$		81	$C_2H_5O^+ \cdot 2H_2O$	✓	✓
	NO^+	$3.0E^{-10}$	100	43	CH_3CO^+	✓	✓
	NO^+	$3.0E^{-10}$		61	$CH_3CO^+ \cdot H_2O$	✓	✓
	NO^+	$3.0E^{-10}$		79	$CH_3\ CO^+ \cdot 2H_2O$	✓	✓
	O^-	$2.5E^{-11}$	89	-43	$C_2H_3O^-$	✓	✓
	O^-	$2.5E^{-11}$	11	-42	$C_2H_2O^-$	✓	✓
	O_2^+	$3.3E^{-9}$	45	43	$C_2H_3O^+$	✓	✓
	O_2^+	$3.3E^{-9}$	55	44	$C_2H_4O^+$		
	OH^-	$7.6E^{-10}$	100	-43	$C_2H_3O^-$	✓	✓
Butyraldehyde	H_3O^+	$1.4E^{-9}$	5	55	$C_4H_7^+$	✓	
	H_3O^+	$1.4E^{-9}$	95	73	$C_4H_9O^+$	✓	
	H_3O^+	$1.4E^{-9}$		91	$C_4H_9O^+ \cdot H_2O$	✓	
	H_3O^+	$1.4E^{-9}$		109	$C_4H_9O^+ \cdot 2H_2O$	✓	
	NO^+	$2.2E^{-9}$	100	71	$C_4H_7O^+$	✓	✓
	O_2^+	$2.3E^{-9}$	65	44	$C_2H_4O^+$	✓	
	O_2^+	$2.3E^{-9}$	35	72	$C_4H_8O^+$	✓	✓
	OH^-	$8.8E^{-10}$	100	-71	$C_4H_6O^-$	✓	✓
Formaldehyde	H_3O^+	$1.3E^{-9}$	100	31	CH_3O^+	✓	✓
	H_3O^+	$1.3E^{-9}$		49	$H_2CO \cdot H^+ \cdot H_2O$	✓	✓
	H_3O^+	$1.3E^{-9}$		61	$(H_2CO)_2 \cdot H^+$	✓	✓
	H_3O^+	$1.3E^{-9}$		67	$H_2CO \cdot H^+ \cdot (H_2O)_2$	✓	✓
	H_3O^+	$1.3E^{-9}$		79	$(H_2CO)_2 \cdot H^+ \cdot H_2O$	✓	✓
Propionaldehyde	H_3O^+	$3.3E^{-9}$	100	59	$C_3H_7O^+$	✓	✓
	H_3O^+	$3.3E^{-9}$		77	$C_3H_7O^+ \cdot H_2O$	✓	✓
	H_3O^+	$3.3E^{-9}$		95	$C_3H_7O^+ \cdot 2H_2O$	✓	✓
	NO^+	$1.7E^{-9}$	100	57	$C_3H_5O^+$	✓	✓
	O_2^+	$2.3E^{-9}$	57	57	$C_3H_5O^+$	✓	✓
	O_2^+	$2.3E^{-9}$	43	58	$C_3H_6O^+$	✓	✓
	OH^-	$9.6E^{-10}$	100	-57	$C_3H_5O^-$	✓	✓

The reactions not marked for scanning are those, which conflict with other productions of the same mass or with secondary reagent ions. The duration of this measurement method is 8 minutes (240 sec. scanning for positive products, 240 sec. for scanning negative ones) with a time limit of 100 ms and a count limit of 100000. After successful calibration of the flow units, the test gas is produced at a constant dosing rate of 2 µL/min (see 3.3.1). The dosing rate is recorded during the entire dosing process with one measured value per second and after the experiment, the exact theoretical concentration is calculated with the averaged dosing rate and the basic gas flow measured by the gas meter. For the liquid aldehydes a calibration series has been developed by changing the split ratio, for formaldehyde by rising the chamber temperature in the permeation oven (Table 23).

Table 23: SIFT-MS Calibration series for aldehydes. Theoretically calculated concentrations.

Calibration level	Split	Acetaldehyde [mg/m³]	Propionaldehyde [mg/m³]	Butyraldehyde [mg/m³]	Oven temperature Formaldehyde [°C]
1	350	0.062	0.071	0.065	60
2	239	0.091	0.103	0.094	65
3	110	0.237	0.234	0.215	70
4	56	0.466	0.460	0.420	73
5	28	0.935	0.925	0.846	76
6	19	1.420	1.411	1.294	80
7	14	1.935	1.919	1.744	85
8	10	2.483	2.609	2.355	90
9	8	2.983	2.949	3.085	95
10	6	3.979	3.930	4.114	100
11	56	0.395	0.542	0.817	90
12	56	0.851	0.000	0.438	90

As soon as the test gas is stable, three DNPH cartridges are loaded for offline-HPLC analysis (3.5.4) and the SIFT-MS measurements are performed simultaneously. The equilibrium setting is shown as an example in Figure 44. As soon as the concentration of the test gas is stable over a period of 10 minutes, sampling is started.

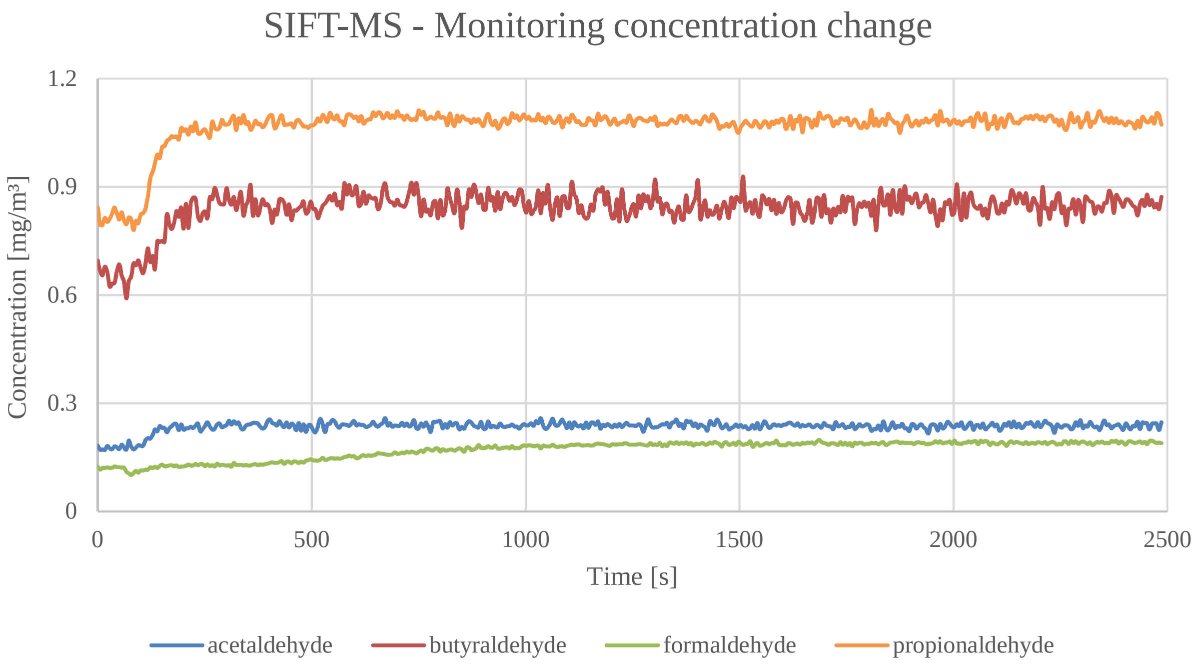


Figure 44: SIFT-MS, monitoring scan changing Concentration from calibration level 6 to 7.

After recording the data, the results of the SIFT measurement are plotted against the calculated concentration and against the results obtained from the HPLC measurement. The diagrams are shown below; the corresponding measured values are given in Appendix 13.

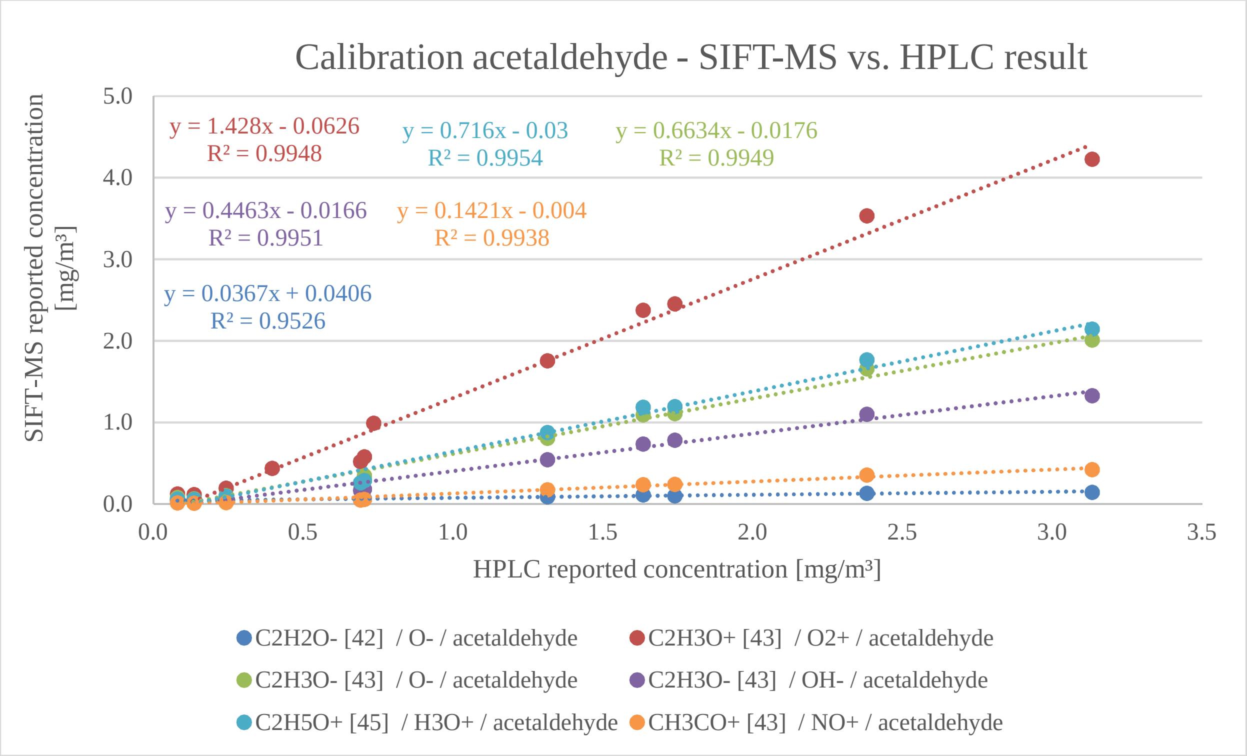


Figure 45: Calibration acetaldehyde - SIFT-MS vs. HPLC result.

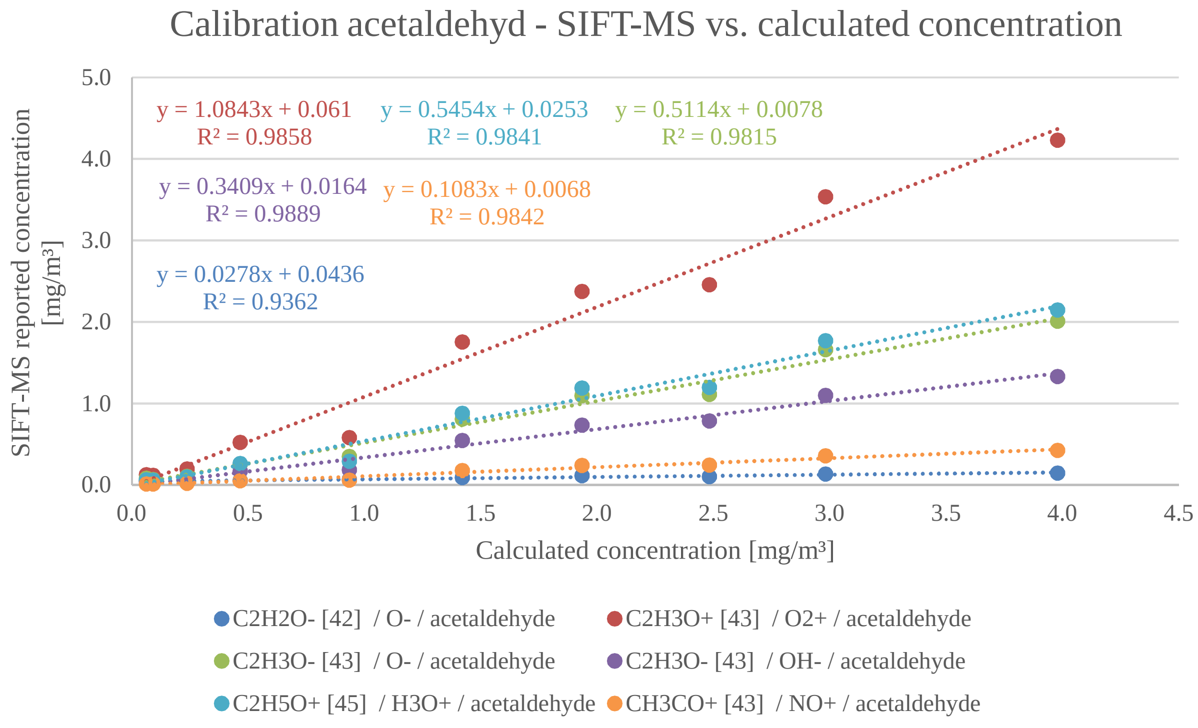


Figure 46: Calibration acetaldehyde - SIFT-MS vs. calculated concentration.

As can be seen, the correlation between the concentrations measured by SIFT-MS and the HPLC results is higher than the correlation between the SIFT-MS results and the calculated concentration. Therefore, the HPLC reported concentration is used as a basis for the calibration, more specifically the calculation of the reaction rate. For propionaldehyde and butyraldehyde, only the correlations between SIFT concentration and the measured HPLC concentration are shown. The diagrams of the SIFT concentration plotted against the calculated concentration can be found in Appendix 14.

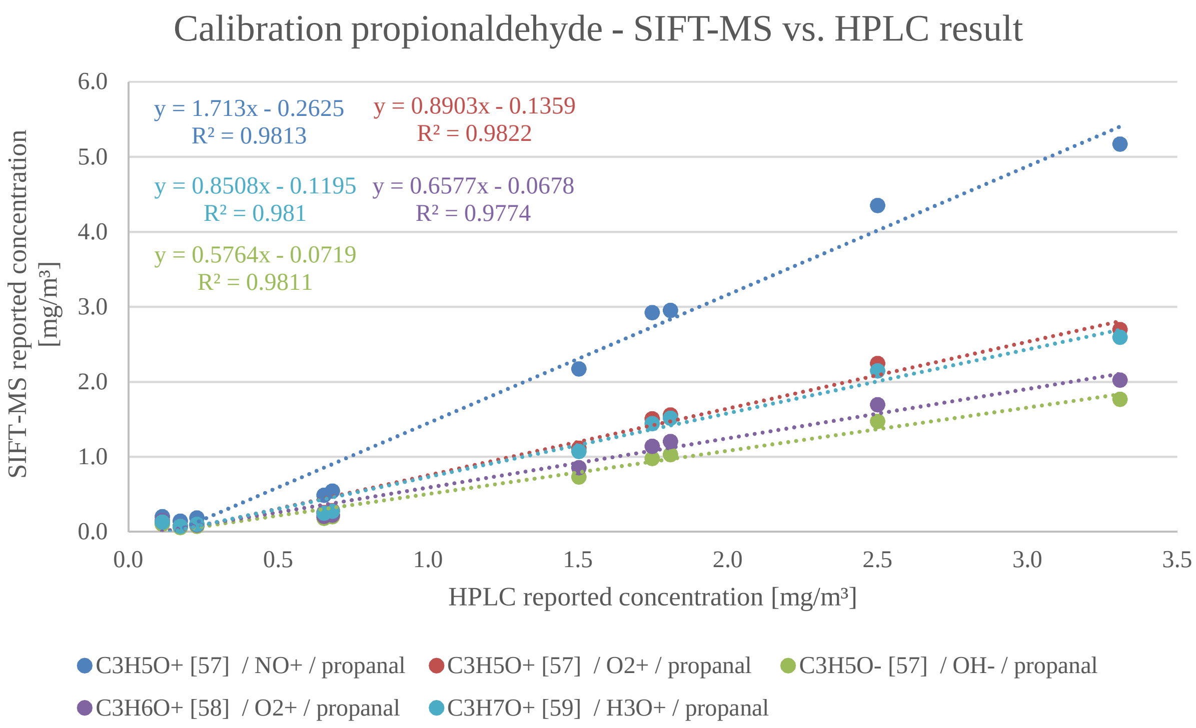


Figure 47: Calibration propionaldehyde - SIFT-MS vs. HPLC result.

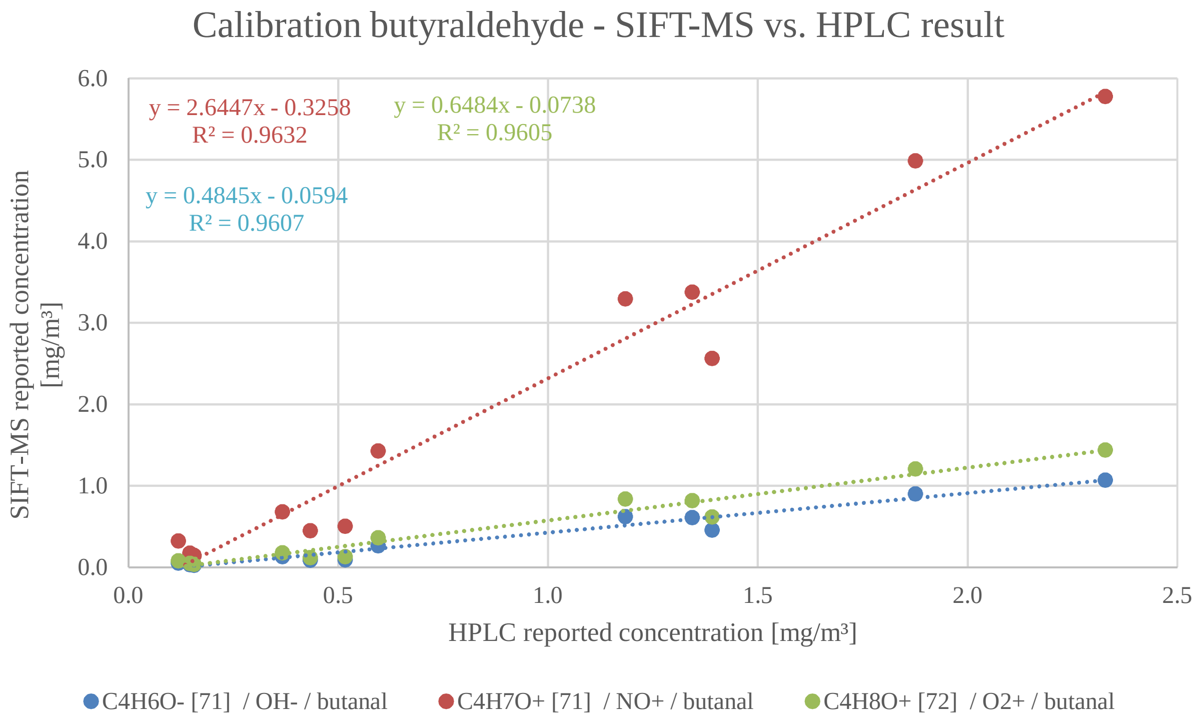


Figure 48: Calibration butyraldehyde - SIFT-MS vs. HPLC result.

No theoretical concentration is calculated for formaldehyde. Instead, the furnace temperature is plotted against the concentration determined by SIFT-MS. To calibrate the SIFT-MS, the SIFT-MS reported concentration is also plotted against the result of the HPLC analysis of the sample carriers.

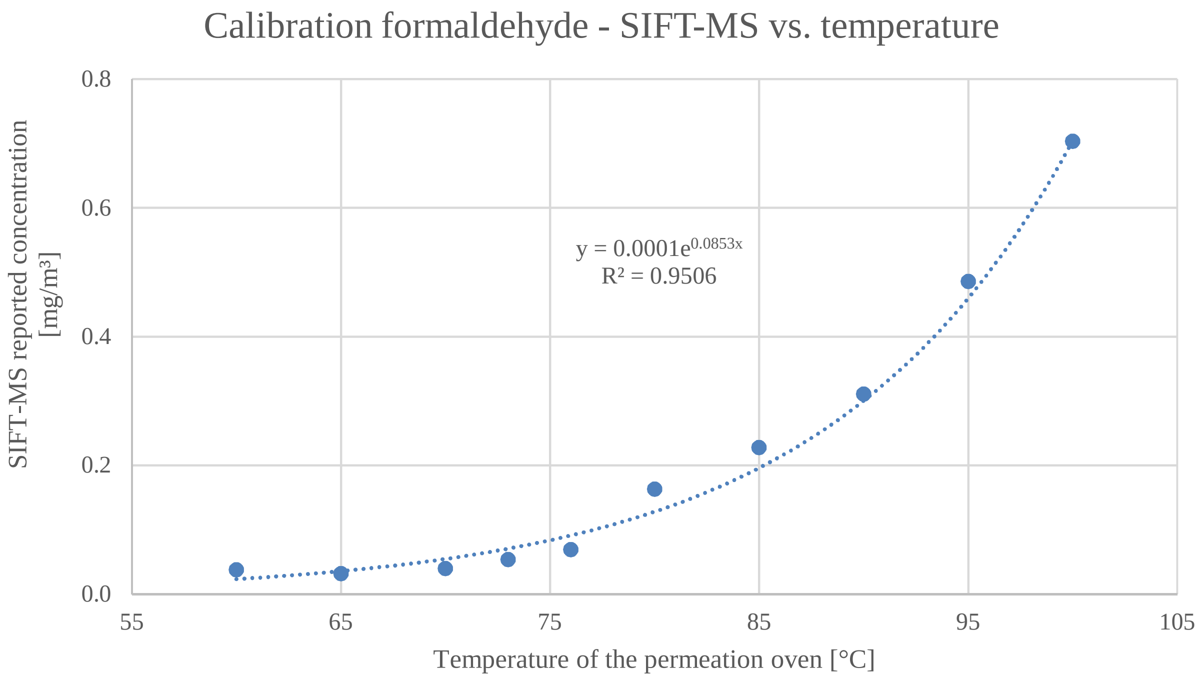


Figure 49: Calibration formaldehyde - SIFT-MS vs. temperature of the permeation oven.

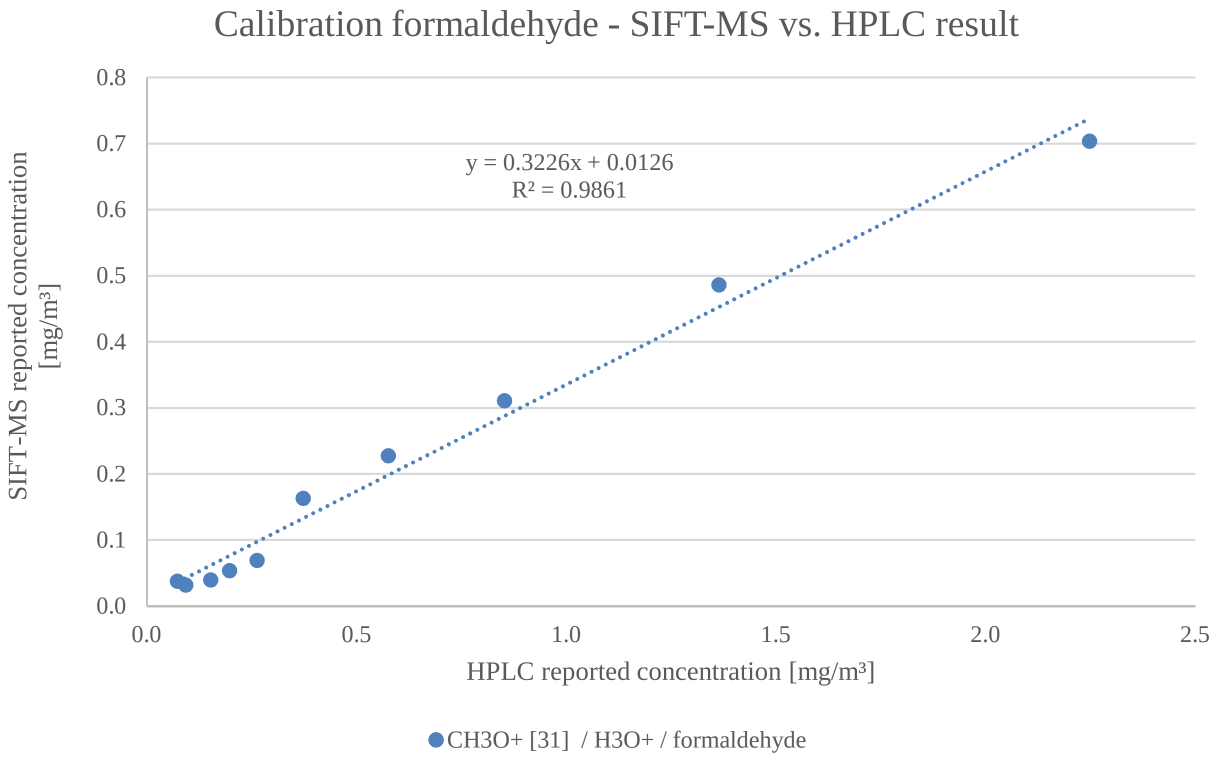


Figure 50: Calibration formaldehyde - SIFT-MS vs. HPLC result

Based on the correlation coefficients, it can be seen that the linear relationship is not sufficiently proven when using all calibration points. Therefore, in the next step, visually recognizable outliers are removed from the calibration function. In addition to the 10 calibration points, two test gases were generated, which approximately correspond to the concentration of the last aldehyde proficiency test, designated as calibration level 11 and 12, see Table 23 and Appendix 13. The following table shows the number of calibration points used for calibration respectively recalculation of the reaction rate for each aldehyde. Furthermore, the table shows the calibration lines for each product ion with their correlation coefficients and the new reaction rates based on them. The new reaction rate is calculated by multiplying the theoretical reaction rate with the slope of the calibration line.

Table 24: Results of the SIFT-MS calibration for aldehyde analysis (per product ion).

	Product ion	Calibration points (n)	Calibration function	r	k (lib.)* [cm^3 molecule^{-1} s^{-1}]	k (calib.)*^{2} [cm^3 molecule^{-1} s^{-1}]
Acetaldehyde	$C_2H_5O^+$ [45] / H_3O^+	10	y = 0.7203x - 0.041	0.9955	$3.40E^{-09}$	$2.45E^{-09}$
	CH_3CO^+ [43] / NO^+		y = 0.1427x - 0.0057	0.9943	$2.10E^{-09}$	$3.00E^{-10}$
	$C_2H_2O^-$ [42] / O^-		y = 0.034x + 0.0477	0.9057	$1.10E^{-10\ **3}$	$2.46E^{-11}$
	$C_2H_3O^-$ [43] / O^-		y = 0.6655x - 0.0232	0.9954		
	$C_2H_3O^+$ [43] / O_2^+		y = 1.428x - 0.0626	0.9948	$2.30E^{-09}$	$3.28E^{-09}$
	$C_2H_3O^-$ [43] / OH^-		y = 0.4481x - 0.021	0.9955	$1.70E^{-09}$	$7.62E^{-10}$
Propionaldehyde	$C_3H_7O^+$ [59] / H_3O^+	8	y = 0.8315x - 0.0537	0.9920	$4.00E^{-09}$	$3.33E^{-09}$
	$C_3H_5O^+$ [57] / NO^+		y = 1.6725x - 0.1281	0.9913	$1.00E^{-09}$	$1.67E^{-09}$
	$C_3H_5O^+$ [57] / O_2^+		y = 0.8673x - 0.0612	0.9917	$3.10E^{-09}$	$2.34E^{-09}$
	$C_3H_6O^+$ [58] / O_2^+		y = 0.6453x - 0.0218	0.9909		
	$C_3H_5O^-$ [57] / OH^-		y = 0.5662x - 0.0345	0.9917	$1.70E^{-09}$	$9.62E^{-10}$
Butyraldehyde	$C_4H_7O^+$ [71] / NO^+	6	y = 2.6692x - 0.1721	0.9922	$8.10E^{-10}$	$2.16E^{-09}$
	$C_4H_8O^+$ [72] / O_2^+		y = 0.6561x - 0.0331	0.9913	$3.50E^{-09}$	$2.30E^{-09}$
	$C_4H_6O^-$ [71] / OH^-		y = 0.4901x - 0.0288	0.9914	$1.80E^{-09}$	$8.82E^{-10}$
Formaldehyde	CH_3O^+ [31] / H_3O^+	10	y = 0.3226x + 0.0126	0.9861	$3.40E^{-09}$	$1.31E^{-09}$

* k(lib)=reaction rate syft library

*^{2} k(calib.)=reaction rate calibrated within this work.

^{**3} no library entry, value based on preceded experiments

For the reaction of acetaldehyde with the reagent ion O^- new branching ratios based on the calibration are also calculated. The same applies to the reaction of O_2^+ with propionaldehyde.

Table 25: Calculated branching ratios for the reaction of acetaldehyde with O^- and propionaldehyde with O_2^+ based on calibration. *Branching ratio of the O^- reaction channel are based on preceded experiments.

Product ion	Branching ratio (syft library)*	Branching ratio (calibrated within this work)
$C_2H_2O^-$ [42] / O^- / acetaldehyde	0.7	0.1
$C_2H_3O^-$ [43] / O^- / acetaldehyde	0.3	0.9
$C_3H_5O^+$ [57] / O_2^+ / propionaldehyde	0.5	0.57
$C_3H_6O^+$ [58] / O_2^+ / propionaldehyde	0.5	0.43

Since the reactions of acetaldehyde with O^- are very slow and there is no sufficient linear relationship between acetaldehyde with O^- and the reaction product $C_2H_2O^-$ [42], these are no longer considered in the further course of method development and are removed from the final measurement method for the online control of aldehydes.

Comparing the theoretically calculated concentrations to those of the analysis of the test gas by HPLC, it is noticeable that the actual concentration is smaller than the calculated concentration. This can either be due to an incorrect dosing or a deviation of the gas flows in the evaporator unit. While the recovery is above 100% at the low calibration levels, it decreases with increasing concentration (Figure 51).

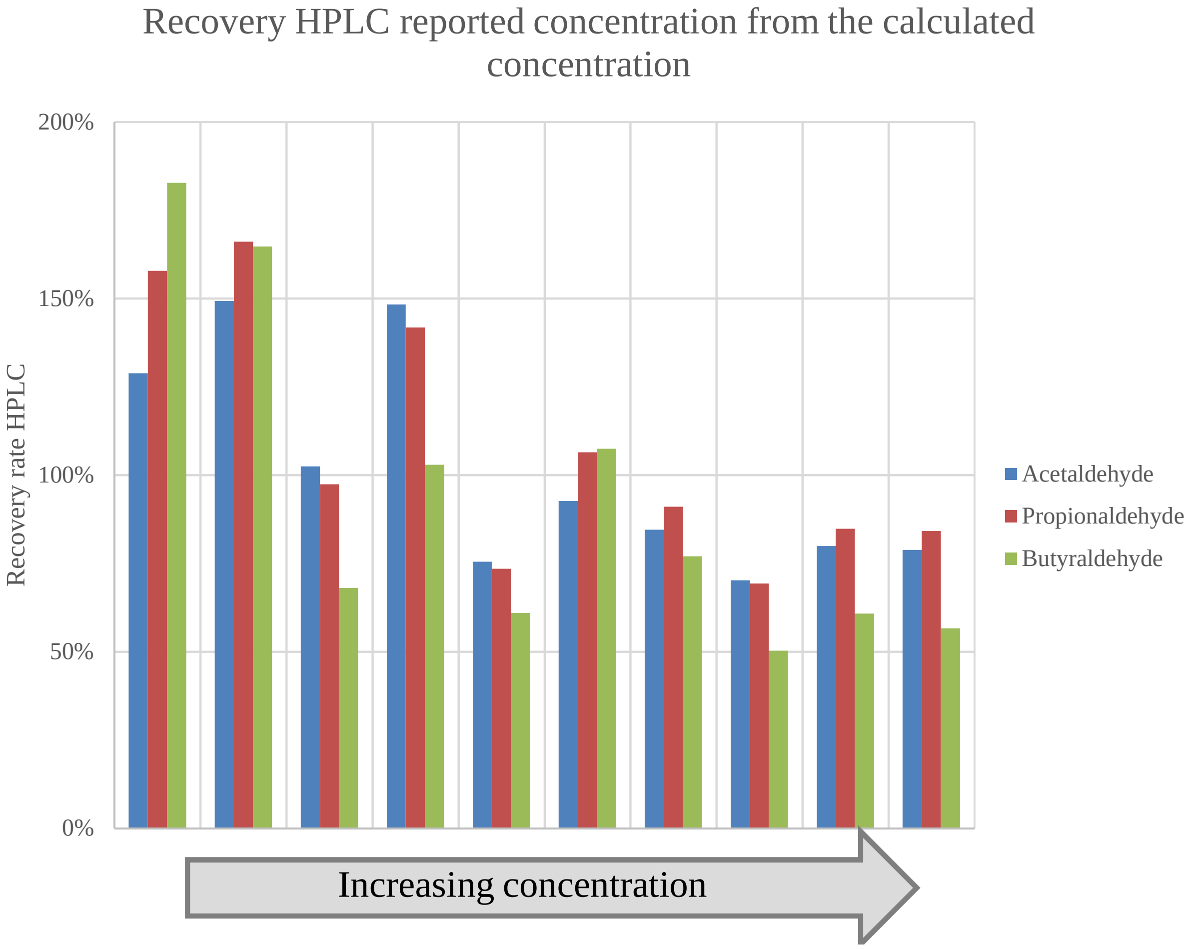


Figure 51: Recovery HPLC from calculated concentration.

Despite outliers, a trend can be detected, which indicates a systematic error. If the HPLC result is plotted against the calculated concentration values (Figure 52) and the outliers are removed, the linear relationship describes the correction function, which is from now on included in the calculation of the theoretical concentration.

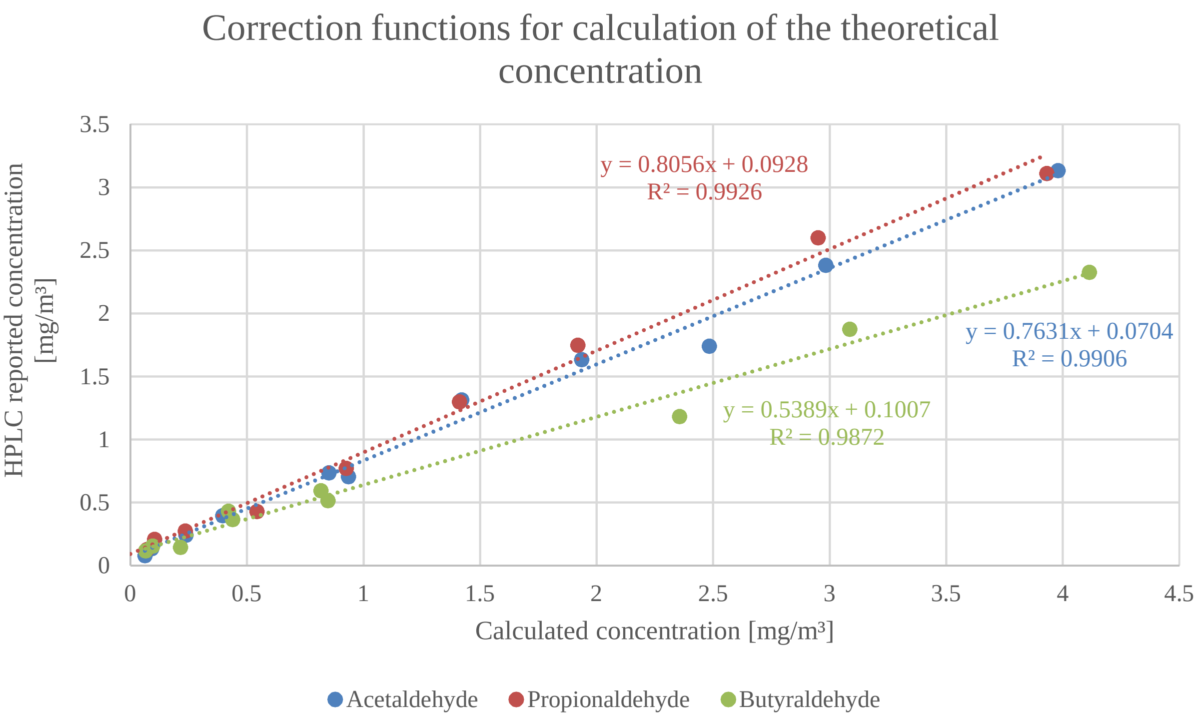


Figure 52: Correction functions for calculation the theoretical concentration of acetaldehyde, propionaldehyde and butyraldehyde.

The adjustment of the concentration by permeation of paraformaldehyde depends exponentially on the temperature, as shown in the following diagram.

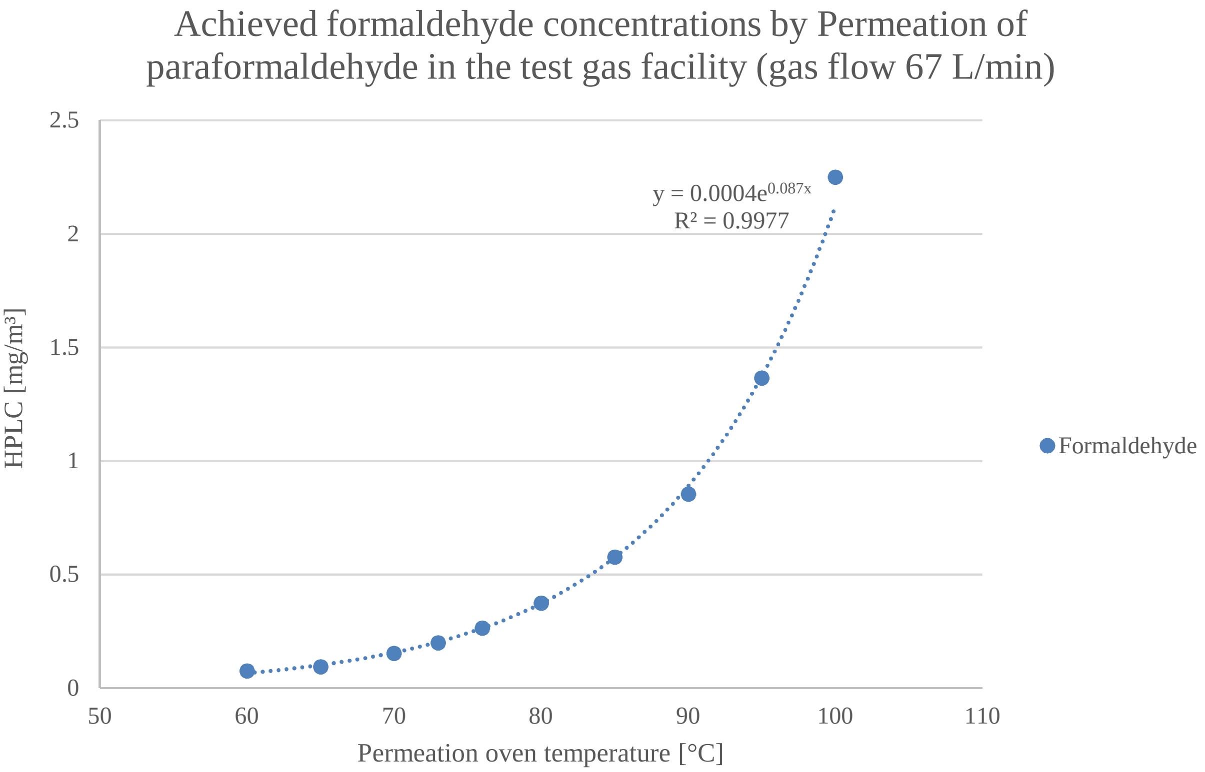


Figure 53: Achieved formaldehyde concentrations in the test gas facility at a basic gas flow of 67 L/min with different tempering of the permeation oven.

5.5.2 Precision test and test on repeatability

After calibration, tests are performed to verify the precision of the dosing process. Therefore, six measurements of three preparations at ~50 % of linear range are being conducted. Relative standard deviation of measurements are calculated to access precision. In addition, the recovery was calculated, which, however, does not serve to assess the precision. To obtain more information about the individual reactions of the aldehydes with different reagent ions, the evaluation of the precision is carried out both for the individual reactions and for the overall result.

Table 26: SIFT-MS precision test for acetaldehyde. Evaluation per product ion.

Product	$C_2H_3O^-$ [43] / OH^- / acetaldehyde			$C_2H_3O^+$ [43] / O_2^+ / acetaldehyde			$C_2H_5O^+$ [45] / H_3O^+ / acetaldehyde			CH_3CO^+ [43] / NO^+ / acetaldehyde		
Preparation	1	2	3	1	2	3	1	2	3	1	2	3
Calculated Conc. [mg/m³]	1.59	1.73	1.75	1.59	1.73	1.75	1.59	1.73	1.75	1.59	1.73	1.75
Reported concentration single measurements [mg/m³]	1.65	1.67	1.63	1.65	1.69	1.72	1.47	1.47	1.54	1.64	1.68	1.73
	1.62	1.67	1.60	1.66	1.49	1.71	1.45	1.28	1.50	1.68	1.50	1.69
	1.52	1.64	1.59	1.64	1.69	1.74	1.43	1.46	1.53	1.65	1.70	1.70
	1.36	1.63	1.61	1.47	1.75	1.74	1.28	1.50	1.54	1.48	1.74	1.74
	1.30	1.65	1.59	1.45	1.72	1.73	1.24	1.49	1.52	1.45	1.71	1.72
	1.19	1.65	1.60	1.21	1.72	1.74	1.04	1.47	1.52	1.21	1.73	1.70
Average [mg/m³]	1.44	1.65	1.60	1.51	1.68	1.73	1.32	1.45	1.53	1.52	1.68	1.71
Standard deviation [mg/m³]	0.17	0.01	0.01	0.16	0.09	0.01	0.15	0.08	0.01	0.16	0.08	0.02
Relative standard deviation [%]	11.7	0.9	0.9	10.6	5.1	0.7	11.5	5.2	0.9	10.7	4.9	1.0
Recovery rate [%]	**90**	**95**	**92**	**95**	**97**	**99**	**83**	**84**	**87**	**95**	**97**	**98**

From the data above, it can be seen that the standard deviation of the first preparation for the precision test is very high compared to the preparations two and three. This can be explained by a very unsteady dosing of the dosing pump (see Table 27) during the first run. Normally, the relative standard deviation of the dosage is below 10 %, less than 5 % in most cases.

Table 27: Evaluation of the dosage during the precision test for acetaldehyde.

Dosage data for Acetaldehyde during precision test			
	P1	P2	P3
Target [µl/min]	2.201	2.201	2.201
Minimum [µL/min]	-94.785	-0.250	0.959
Maximum [µL/min]	12.622	3.957	2.652
Average [µL/min]	2.176	2.190	2.199
Standard deviation [µL/min]	3.112	0.380	0.096
Relative standard deviation [%]	**143**	**17**	**4**

Looking at the data of Propionaldehyde (Table 28), the (relative) standard deviations of the three preparations are much more homogenous than for acetaldehyde. Although an increased standard deviation in the dosage was recorded for preparation 2 (see Table 29), this cannot be seen from the measured values, see the table below. The only striking feature of the data is the poor recovery for preparation 3, which is clearly too high. A reason for this could not be found when the data was reviewed and calculated again. This indicates a random error from the dosing process.

Table 28: SIFT-MS precision test for propionaldehyde. Evaluation per product ion.

Product	$C_3H_5O^-$ [57] / OH^- / propionaldehyde			$C_3H_5O^+$ [57] / NO^+ / propionaldehyde			$C_3H_5O^+$ [57] / O_2^+ / propionaldehyde			$C_3H_6O^+$ [58] / O_2^+ / propionaldehyde			$C_3H_7O^+$ [59] / H_3O^+ / propionaldehyde		
Preparation	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
Calculated conc. [mg/m³]	1.89	1.89	1.78	1.89	1.89	1.78	1.89	1.89	1.78	1.89	1.89	1.78	1.89	1.89	1.78
Reported concentration single measurements [mg/m³]	1.66	1.69	2.87	1.6	1.65	2.88	1.54	1.57	2.72	1.66	1.67	2.96	1.45	1.46	2.68
	1.67	1.71	2.83	1.64	1.71	2.90	1.55	1.61	2.76	1.69	1.73	2.99	1.5	1.47	2.68
	1.66	1.73	2.86	1.66	1.74	2.93	1.58	1.65	2.79	1.70	1.74	3.03	1.52	1.48	2.70
	1.69	1.73	2.91	1.70	1.74	3.00	1.59	1.65	2.84	1.73	1.74	3.10	1.51	1.50	2.74
	1.68	1.67	2.88	1.69	1.73	2.95	1.61	1.64	2.81	1.73	1.71	3.02	1.49	1.50	2.68
	1.69	1.68	2.90	1.70	1.7	3.01	1.61	1.62	2.85	1.73	1.73	3.10	1.48	1.49	2.74
Average [mg/m³]	1.68	1.70	2.88	1.67	1.71	2.95	1.58	1.62	2.80	1.71	1.72	3.03	1.49	1.48	2.70
Standard deviation [mg/m³]	0.01	0.02	0.03	0.04	0.03	0.05	0.03	0.03	0.05	0.03	0.02	0.05	0.02	0.01	0.03
Relative standard deviation [%]	0.8	1.4	0.9	2.2	1.8	1.6	1.7	1.7	1.6	1.5	1.4	1.7	1.5	1.0	1.0
Recovery rate [%]	**89**	**90**	**161**	**88**	**91**	**165**	**84**	**86**	**157**	**90**	**91**	**170**	**89**	**90**	**161**

Table 29: Evaluation of the dosage during the precision test for propionaldehyde.

Dosage data for Propionaldehyde during Precision test			
	P 1	P 2	P 3
Target [µl/min]	2.134	2.134	2.001
Minimum [µL/min]	1.878	1.228	1.506
Maximum [µL/min]	2.774	4.231	2.392
Average [µL/min]	2.135	2.130	2.000
Standard deviation [µL/min]	0.096	0.339	0.083
Relative standard deviation [%]	4.5	16	4.2

In contrast, looking at the results of the precision test of butyraldehyde (Table 30 and Table 31), a correlation between the standard deviation of the dosage and that of the precision tests can be seen. Here it is clearly shown that the stability of the dosage has a decisive influence on the precision of the concentration measurement.

Table 30: SIFT-MS precision test for butyraldehyde. Evaluation per product ion.

Product	$C_4H_6O^-$ [71] / OH^-/ butyraldehyde			$C_4H_7O^+$ [71] / NO^+ / butyraldehyde			$C_4H_8O^+$ [72] / O_2^+ / butyraldehyde		
Preparation	1	2	3	1	2	3	1	2	3
Calculated conc. [mg/m³]	1.16	1.16	1.32	1.16	1.16	1.32	1.16	1.16	1.32
Reported concentration single measurements [mg/m³]	1.09	1.1	1.39	1.07	1.08	1.48	1.09	1.1	1.43
	1.08	1.09	1.38	1.09	1.16	1.47	1.08	1.18	1.42
	1.09	1.11	1.39	1.1	1.13	1.48	1.12	1.15	1.43
	1.1	1.14	1.40	1.13	1.11	1.51	1.14	1.12	1.49
	1.12	1.11	1.38	1.13	1.12	1.49	1.14	1.14	1.45
	1.09	1.12	1.42	1.12	1.09	1.49	1.12	1.13	1.47
Average [mg/m³]	1.10	1.11	1.39	1.11	1.12	1.49	1.12	1.14	1.45
Standard deviation [mg/m³]	0.01	0.02	0.01	0.02	0.03	0.01	0.02	0.02	0.02
Relative standard deviation [%]	1.1	1.4	1.0	2.0	2.4	0.8	2.1	2.2	1.7
Recovery rate [%]	**94**	**96**	**106**	**95**	**96**	**113**	**96**	**98**	**110**

Table 31: Evaluation of the dosage during the precision test for butyraldehyde.

Dosage data for Butyraldehyde during Precision test			
	P 1	P 2	P 3
Target [µl/min]	1.973	1.973	2.255
Minimum [µL/min]	0.581	0.230	1.608
Maximum [µL/min]	3.430	4.049	2.773
Average [µL/min]	1.962	1.959	2.248
Standard deviation [µL/min]	0.406	0.486	0.118
Relative standard deviation [%]	21	25	5.2

The results of the evaluation per product ion coincide with those of the evaluation per analyte, which is to be expected. These data can be seen in Appendix 15.

In conclusion, it can be stated that the precision of the results depends less on the actual measurement but significantly on the stability and precision of the dosage. This is an obviously logical connection, but this fact should not remain unmentioned, since it is not yet known why the dosage sometimes varies greatly, which can be seen from the standard deviation of the dosage process. It should be clarified what influences the pumps and the precision of the dosing rate. This is essential for the successful and reliable use of the dosing system. Apart from this, it can be stated that the precision of the analytical measurement is proven with relative standard deviations of mostly less than 2%.

5.5.3 Robustness

As described in chapter 4.3.1, the test for robustness is used to check to what extent the temperature of the inlet and the flow tube temperature have an influence on the measurement result. The tolerance of the measuring instrument is ± 7 °C from the target value (120°C). The test conditions and the results are shown in the following Table 32. The recovery is based on the measured concentration under ideal conditions of 120°C flow tube and inlet temperature (reference value). The associated measured values for evaluation are listed in Appendix 16.

Table 32: SIFT-MS validation: Results of the test for robustness.

	% recovery to reference value			
	Robustness Test 1	Robustness Test 2	Robustness Test 3	Robustness Test 4
	Flow tube 120 °C, Inlet 127 °C	Flow tube 120 °C, Inlet 113 °C	Flow tube 113 °C, Inlet 120 °C	Flow tube 127 °C, Inlet 120 °C
Acetaldehyde	97.0	104.3	100.3	92.5
Butyraldehyde	96.4	103.5	100.3	95.9
Formaldehyde	95.9	101.2	100.7	96.0
Propionaldehyde	97.1	104.3	100.5	97.3

The results confirm the theory of quantification in SIFT-MS (2.2.3). The temperature change slightly alters the reaction rate and thus the measured concentrations under the changed temperature conditions differ from those measured under the ideal conditions of 120 °C. The effect of the temperature change is the same for all substances, but in some cases to a different extent. For example, when the inlet temperature is increased from 120 °C to 127 °C, the recovery of the reference value is reduced to the same extent for all four analytes, whereas when the flow tube temperature is increased from 120 °C to 127 °C, acetaldehyde appears to be affected to a greater extent than the other aldehydes. Whether this is an accidental deviation would have to be checked with a larger series of experiments. As deviations of <8 % are involved and deviations of the device parameters to this extent are not to be expected on a daily basis, no further tests are carried out.

5.5.4 The influence of relative humidity on aldehyde analysis using SIFT-MS

In contrast to the device parameters flow tube temperature and inlet temperature, the test for the influence of relative humidity is a parameter, which is deliberately varied e.g. in the context of method development. The relative humidity during calibration is 30-33 %, which corresponds to usual conditions of the proficiency test. The fact that the SIFT-MS results depend on the humidity of the sample is already evident when looking at the theoretical background and that has been published. Since the influence of the humidity on the result depends on the analyte as well as on the selected reagent ion and the extent is unknown, the results of the experiments on the variation of the humidity in the test gas facility and its influence on the measured aldehyde concentration are shown.

In order to quantitatively illustrate the influence of humidity for the intended application, the test gas is measured once at the humidity of the calibration as a reference and then the humidity is increased or decreased. The tests are performed at 6 % and 69 % relative humidity, compared to the reported concentration at 33 %. The influences of the result per reagent ion are evaluated as well as the total concentration.

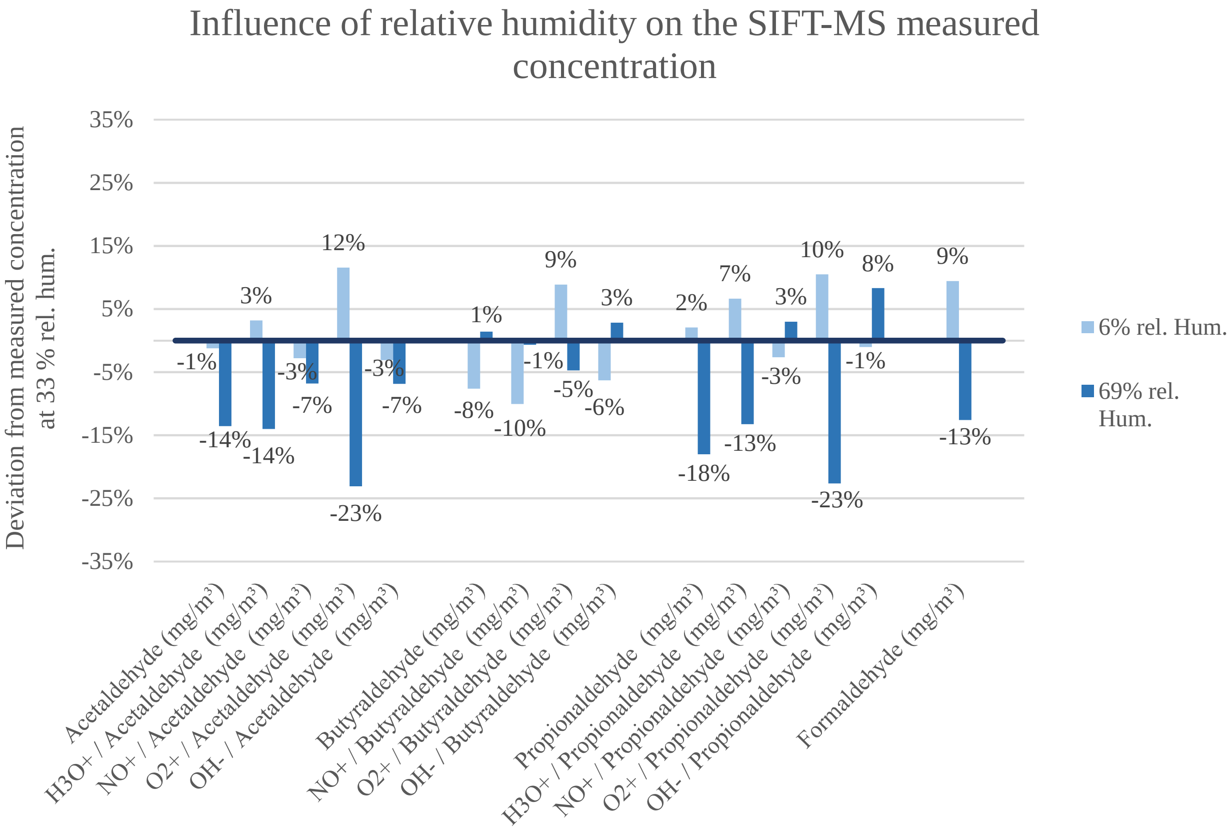


Figure 54: Influence of relative humidity on the SIFT-MS measured concentration. Deviation of measurement at 6 % and 69 % rel. humidity from measured reference measurement at 33 % rel. humidity.

Looking at the percentage deviations of the measured concentrations at the changed humidity from the results at the reference of 33 %, it is initially noticeable that for butyric aldehyde, which is the longest chained aldehyde in the experiment, the effect of humidity is least pronounced. Furthermore, on the basis of the measured data, the theory that the influence of the secondary ion chemistry is least pronounced in reactions with the reagent ion NO^+ and OH^- can be confirmed. For both acetaldehyde and propionaldehyde the effect of the secondary ion chemistry is strongest in reactions with O_2^+, but is also significantly pronounced in reactions with H_3O^+. By evaluating the raw data (in Hz), the already known influence, described in section 2.2.3 of sample humidity on secondary ion formation could be confirmed and additionally quantified. For example, the formation of $H_3O^+{\cdot}H_2O$ (m/z = 37), the first water cluster of H_3O^+ (m/z = 19), increases by 40.5% when the relative humidity in the sample increases from 6% to 69%. The relationship is linear.

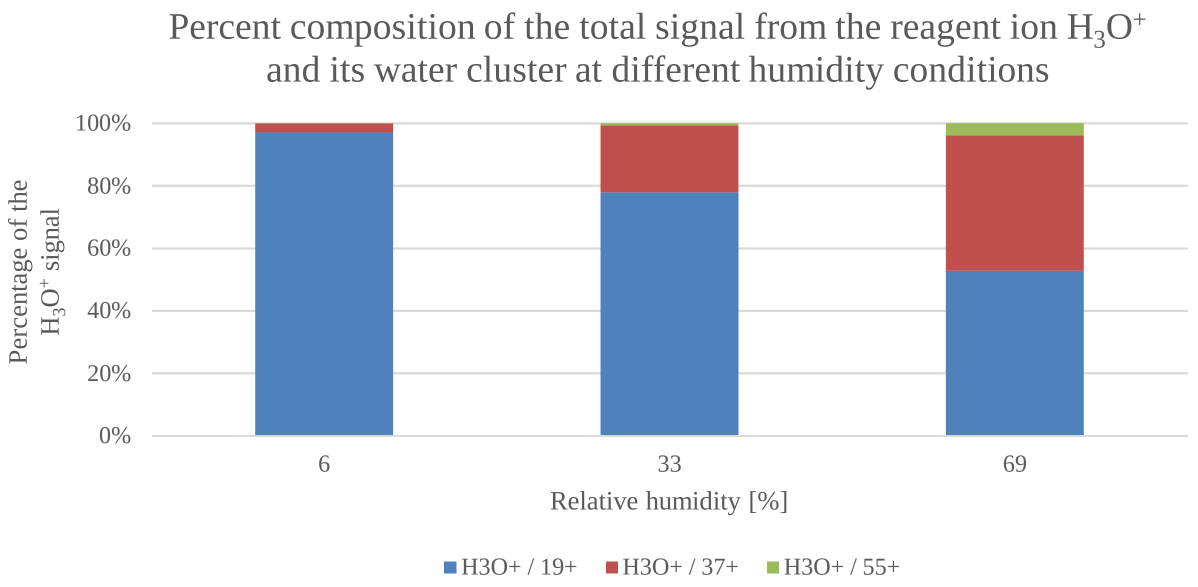


Figure 55: Percentage composition of the total signal from the reagent ion H_3O^+ and its water cluster at different humidity conditions.

Corresponding to the increase in water clusters formation of the reagent ions at high humidity conditions, the formation of secondary product ions also increases with increasing humidity. The following figure shows the composition of the H_3O^+ signal when measuring acetaldehyde under different humidity conditions.

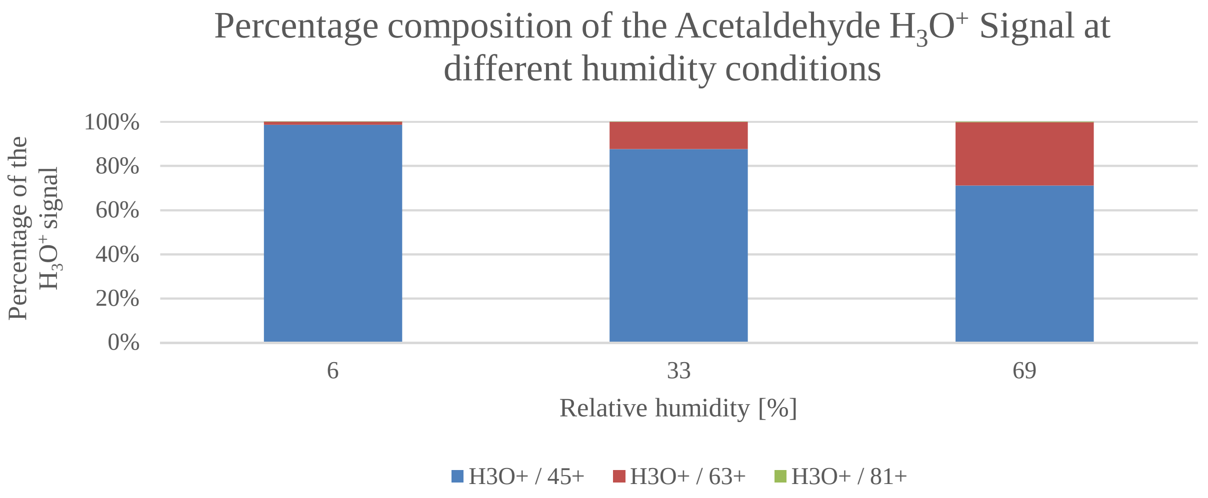


Figure 56: Percentage composition of the H_3O^+ Signal for aldehyde at different humidity conditions.

In comparison, the formation of secondary ions of NO^+ under high relative humidity is very low as shown in Figure 57. The formation of the $NO^+•H_2O$ water cluster only increases by 1.3%.

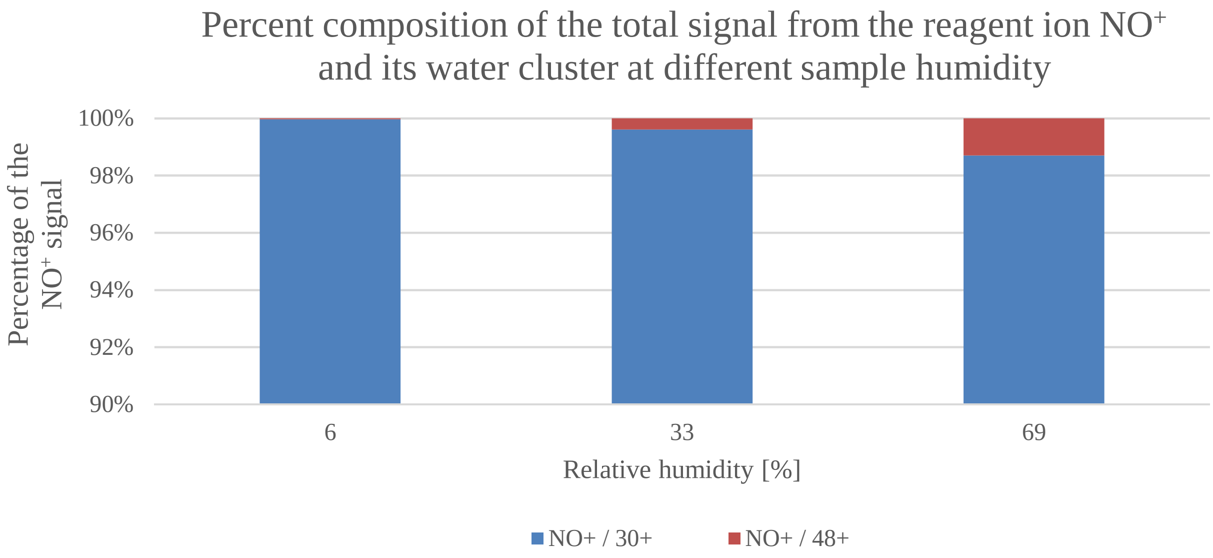


Figure 57: Percentage composition of the total signal from the reagent ion NO^+ and its water cluster at different sample humidity.

OH^- shows a very similar behavior in the formation of water clusters as shown in the following figure.

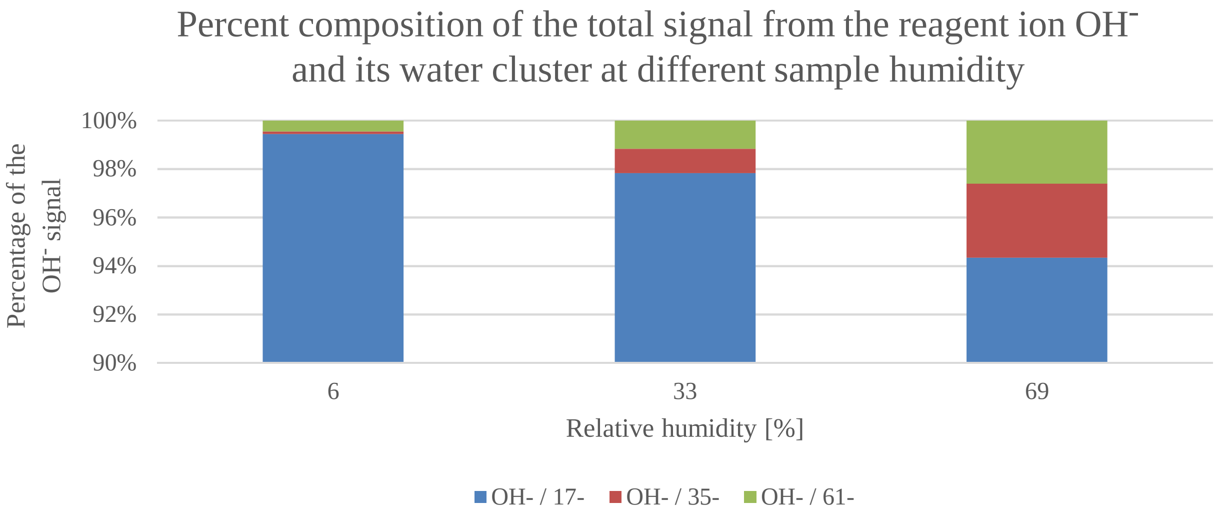


Figure 58: Percentage composition of the total signal from the reagent ion OH^- and its water cluster at different sample humidity.

As expected, the formation of the secondary ions of the product ions increases with increasing relative humidity. However, the influence on the total signal is less than 2 %. Thus, the quantification with NO^+ and OH^- is robust against humidity influences.

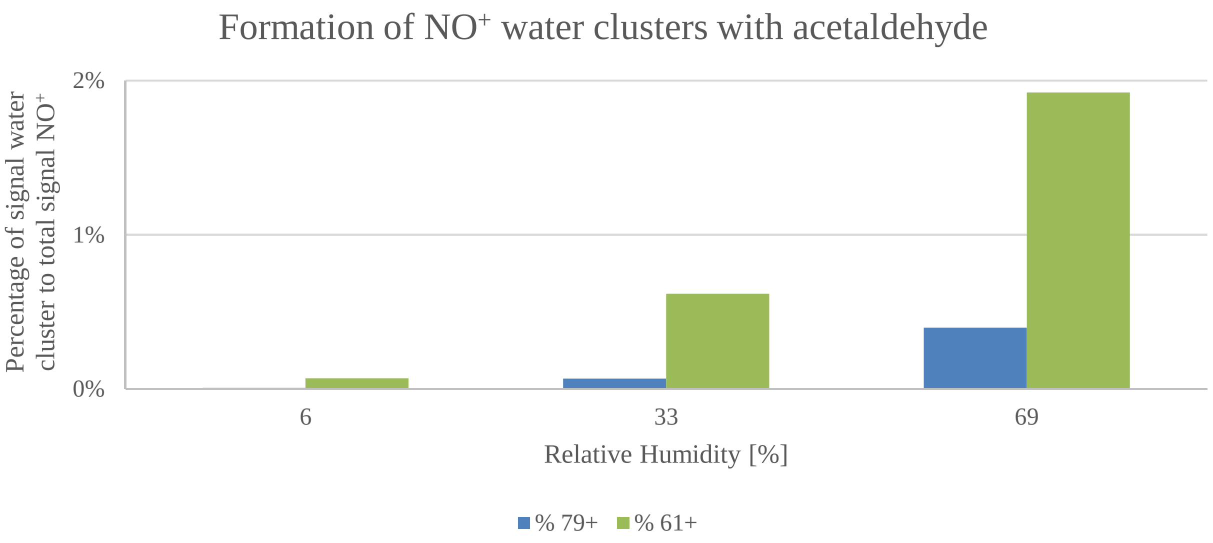


Figure 59: Secondary product ion formation of NO^+ with acetaldehyde.

In contrast to H_3O^+, the secondary reactions of the reagent ion O_2^+ are not fully understood. As already described in Chapter 2.2.2, H_3O^+ reaction ion peaks in the O_2^+ spectrum form at increased humidity. These signals are therefore not included in the quantification of the O_2^+ signal, which is why it leads to an underreported concentration at elevated humidity, more than the other reagent ions do under high humidity conditions in general. Potentially generated O_2^+ secondary product ions are not measured. It can also be observed that with propionaldehyde, the analyte concentration in the O_2^+ channel is more strongly reduced than with butyraldehyde. The reason for this is that with propionaldehyde, two O_2^+ product ions are measured, which lead to varying degrees of reduced results, see Table 33.

Table 33: Different influence of humidity on O_2^+ product ions with propionaldehyde.

	Propionaldehyde concentration per product ion			
	33 % humidity		69 % humidity	
	concentration [$\mathrm{mg/m^3}$]	deviation in O_2^+ channel [%]	concentration [$\mathrm{mg/m^3}$]	deviation in O_2^+ channel [%]
$C_3H_5O^+$ [57] / NO^+	3.02		3.11	
$C_3H_5O^+$ [57] / O_2^+	2.85	-7.77	2.29	-21.03
$C_3H_6O^+$ [58] / O_2^+	3.09		2.90	
$C_3H_5O^-$ [57] / OH^-	2.90		3.14	
$C_3H_7O^+$ [59] / H_3O^+	2.86		2.48	

Due to the set tolerance of 20 % for excess findings, the higher displayed concentration (2.90 $\mathrm{mg/m^3}$) is not included in the calculation of the concentration value per reagent ion and therefore in the analyte concentration. Because the deviation of the reported concentrations with O_2^+ at 33 % humidity is below 20 %, the reported concentration per reagent ion and per analyte is not affected the same way. For the same reason, the total concentration per analyte is also underreported, since the less affected product ions resulting from the reactions with NO^+ and OH^- are not included in the total concentration due to the set tolerance of 20 % for excess findings.

Although both, primary and secondary ion formation of H_3O^+ and the corresponding productions are well understood, quantification of H_3O^+ at elevated humidity results in an underestimation of >10% in this sample. The reason for this could be that secondary ion formation cannot be predicted as accurately as primary ion formation. For this reason, it is also not recommended to quantify ions exclusively via the secondary product ions.

Increasing the tolerance leads to a less strong deviation, but due to the large number of product ions that can be used for quantification, the reactions can be removed from the quantification for propionaldehyde and acetaldehyde using O_2^+ and H_3O^+.

In the final method, the reactions of the following reagent ions with their corresponding product ions are therefore used for quantification of aldehydes.

Table 34: Final method for the determination of aldehydes in test gases using SIFT-MS. Selected ion molecule reactions for quantification.

Compound	Reagent ion	Reaction rate k [cm^3 $molecule^{-1}$ s^{-1}]	Mass (m/z)	Product
Formaldehyde	H_3O^+	$1.30E^{-09}$	31	CH_3O^+
			49	$H_2CO•H^+•H_2O$
			61	$(H_2CO)_2•H_2O$
			67	$H_2CO•H^+•(H_2O)_2$
			79	$(H_2CO)_2•H^+•H_2O$
Acetaldehyde	NO^+	$3.00E^{-10}$	43	CH_3CO^+
			61	$CH_3CO^+•H_2O$
			79	$CH_3CO^+•2H_2O$
	OH^-	$7.60E^{-10}$	-43	$C_2H_3O^-$
Propionaldehyde	NO^+	$1.70E^{-09}$	57	$C_3H_5O^+$
	OH^-	$9.60E^{-10}$	-57	$C_3H_5O^-$
Butyraldehyde	NO^+	$2.20E^{-09}$	71	$C_4H_7O^+$
	O_2^+	$2.30E^{-09}$	72	$C_4H_8O^+$
	OH^-	$8.80E^{-10}$	-71	$C_4H_6O^-$

5.5.5 Variation of the concentration by changing the dosing rate at constant split ratio

The measurement method developed for long time scans quantifies the aldehydes with less product ions than the final method described in Table 34. This method is applied in positive ion mode with the previously determined calibrated reaction rates. It is to be tested whether a concentration change in the test gas by varying the dosing rate of the pressure pumps at a constant split ratio of the evaporator unit can be achieved. The following figure shows the achieved concentration curve. The table below summarizes the measurement results for the individual periods.

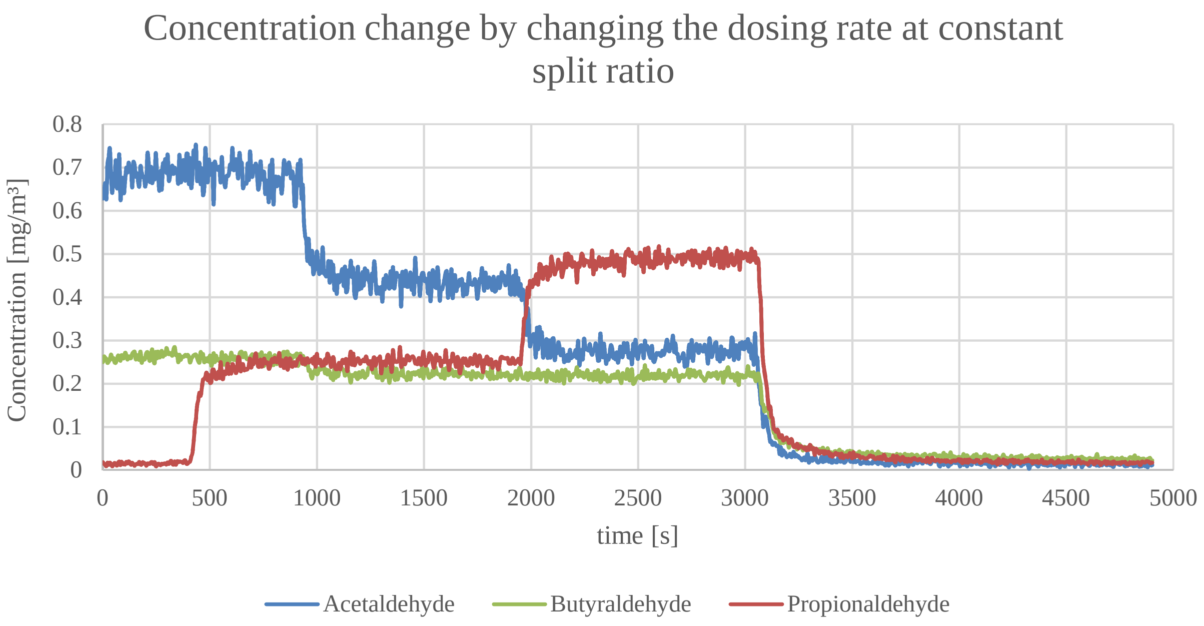


Figure 60: Concentration change by changing the dosing rate at constant split ratio.

Table 35: Quantitative evaluation of the test for variation of aldehyde concentration by changing the dosing rate

Evaluation period	flow rate [µL/min]	Compound	Average [mg/m³]	Calculated concentration [mg/m³]	Recovery rate [%]
100-371	3.8	acetaldehyde	0.69	0.72	96
	0.0	propionaldehyde	0.00	0.00	-
	2.0	butyraldehyde	0.27	0.34	79
730-915	3.8	acetaldehyde	0.67	0.72	94
	1.6	propionaldehyde	0.25	0.38	65
	2.0	butyraldehyde	0.26	0.34	77
1370-1830	2.5	acetaldehyde	0.43	0.49	88
	1.6	propionaldehyde	0.25	0.38	66
	1.7	butyraldehyde	0.22	0.31	73
2450-3020	1.7	acetaldehyde	0.28	0.36	77
	2.9	propionaldehyde	0.49	0.62	79
	1.7	butyraldehyde	0.22	0.31	72

As shown in the figure, concentration changes in the test gas can be realized in a very short time by varying the dosing rate with the described setup (Chapter 3.3.4). Nevertheless, the recovery deviates from the defined tolerance range of 20%. The correction factor described above was applied to the theoretically calculated concentrations. However, this factor was determined on the basis of the calibration, in which constant dosing rate and changed split ratios are used. To be able to make a conclusive statement, further experiments must be carried out on the dosing unit.

6 Conclusion and future work

Workplace measurements make an important contribution to the prevention of occupational diseases. According to §7 of the German Hazardous Substances Ordinance, the employer must ensure that the air in workplaces complies with Occupational Exposure Limits (OELs) for hazardous substances.

Due to new findings in toxicology, limit values are being lowered more and more, thus increasing the demands on analytical measurement methods. The Institute for Occupational Safety and Health develops measurement methods and carries out emission measurements itself. In order to ensure the quality of the emission measurements, the IFA operates a dynamic test gas facility to generate test gas atmospheres for workplace measurements. This is used to develop new methods, to test sampling systems and to conduct proficiency tests. The generated test gas atmospheres have to meet high requirements regarding correctness, homogeneity, precision and stability.

The objective of this thesis was to ensure the quality of the test gas by high-resolution online analysis. For this purpose, measurement technology was implemented in the process of generating test gas atmospheres and different analytical methods were developed. Second research topic was the generation of test gas atmospheres for analytes with high vapor pressures and low boiling points from pure substances. Therefore, a new dosing system was designed, consisting of a precise dosing pump with cooled flow path for the realization of small, precise dosing rates coupled with typical GC-injector used as evaporator.

For quality assurance of the VOC test gases a gas chromatographic system was used, which was converted for active gas sampling by special modifications. For the determination of VOCs in the µg/m³ range, an analytical method with prior enrichment of the test gas via thermal desorption was developed. Test gas atmospheres in this concentration range simulate indoor workplaces in the range of 10-200 µg/m³ per substance. A second method was developed for the determination of VOCs in the mg/m³ range, which is used to investigate test gas atmospheres simulating workplaces where work with organic solvents is performed. The concentration range depends on the OELs and extends, depending on the substance, from the single-digit mg/m³ range to the 3 or even 4-digit mg/m³ range. A preconcentration of the test gas is not necessary in this concentration range. The injection technique for this method is a 250 µL sample loop. The main requirements for the developed online analytical methods are highest possible selectivity at short analysis time. By using short capillary columns with very small inner diameters, a fast but still selective separation of the substances can be achieved. The final method for online determination of VOCs in the µg/m³ range with preceding preconcentration leads to an analysis time of 13.6 minutes. Currently, 23 substances in the range of 10-200 µg/m³ can be measured. The limit of quantification for 18 of the 23 substances is below 4 µg/m³. 2-Ethoxyethyl acetate has the highest LOQ with 86 µg/m³, followed by 2-ethoxyethanol with 15 µg/m³.The method was found to be largely robust against humidity. Only very high humidity leads to a significant decrease of recovery for some substances. Due to the absence of preconcentration for the determination of organic solvents in the mg/m³ range, the running time of this measuring method is only 5.8 minutes. The retention times of 33 substances were determined and the method was successfully used for the proficiency test. The measurements of the quality control samples during the proficiency test showed very good results and can be considered equivalent to the offline method. There are some minor limitations in selectivity considering the short analysis time.

In conclusion, it can be stated that the gas chromatographic measuring methods developed are suitable for online monitoring of solvent test gases in the mg/m³ range and VOC test gases in the µg/m³ range. With regard to the variety of substance classes used e. g. in the proficiency tests and the shortest possible analysis time required for online measurement methods, there are minor limitations that should be kept in mind and taken into account when selecting the substances for the respective test gases.

In addition to online gas chromatographic monitoring, the technique of selected ion flow tube mass spectrometry (SIFT-MS) is introduced to the process of test gas generation. Its application allows a continuous monitoring of the quantitative test gas composition in real time. The SIFT-MS technique is based on ultra-soft, precisely controlled chemical ionization (CI) that leads to simplified, reproducible mass spectra, which allows a separation-free analysis. The developed SIFT-MS method for the determination of VOC concentrations in the µg/m³ range was successfully applied in parallel to the online GC. The recovery rate of the calibrated substances is >80 %. However, the SIFT-MS technique also has limitations in terms of selectivity. Affected substances have to be determined as sum concentrations.

Apart from the monitoring of the VOC proficiency test, the SIFT-MS method plays an important role in the second part of this work. This part does not mainly deal with the analysis of test gases but with their production. In particular it is about the production of test gas atmospheres of low boiling components with high vapor pressures. The system is intended to be applicable for many substances, but is first be applied to the aldehydes acetaldehyde, propionaldehyde and butyraldehyde, which are the subject of the proficiency test “Aldehydes”. The new system is intended to replace the previous dosing using a syringe feeder. The system has to meet some special requirements to be used for the test gas production of substances with high vapour pressures at the dynamic test gas facility:

- precise dosing in the nanoliter range,
- due to the high vapor pressure, cooling of the flow path to avoid bubble formation,
- reproducible, quantitative evaporation

A commercially available system, which meets these requirements could not be found. By combining three individual components, a novel system for the generation of test gases was developed. The system is composed of a pump, a high-precision cooling unit and a modified gas chromatographic evaporation system and is suitable for the production of aldehyde test gases with the required quality in connection with the dynamic test gas facility. The used pumps work according to the principle of pressure-based flow control. In combination with a flow meter the control unit works in a feedback loop, physically separated from reservoir and flow path of the component to be dosed. This allows cooling of the parts in contact with the liquid, without affecting the electronics of the control unit. Since the micro pressure pumps dose the aldehydes only in the single digit µl range with the required precision, an intermediate dilution of the test gas must be achieved before the vaporized analyte stream is introduced into the test gas facility. This could be realized by using a modified split-splitless injector system from gas chromatography. The necessary modifications according to the requirements to operate the injector as a stand-alone device were implemented. By the split mode it is possible to vaporize and divide the dosed analyte flow. Only a small part of the analyte gas is then passed through an unfilled capillary column as retention gap at the outlet of the vaporizer into the dynamic test gas facility. The concentration of the test gas is thus determined by the dosing rate, the spit ratio and the dimensions of the capillary column.

SIFT-MS and classical HPLC offline analysis were used to monitor the interaction of the components analytically. Using SIFT-MS, the composition of the test gas could be observed semi-quantitatively in real time. This allows the determination of the optimal dosing parameters. Using the analytical results of the validated HPLC method, the SIFT-MS method for the determination of aldehydes was used to adjust the reactions rates of the aldehydes with various reagent ions. The developed SIFT-MS method was tested for robustness against changes in device parameters and humidity of the test gas. As studies have already shown [82], the SIFT-MS technique is partially sensitive to humidity.

Due to the varying tendency of different reagent ions to undergo secondary chemistry, some reagent ions are more affected by the influence of humidity than others are. Based on the easily controlled conditions in the dynamic test gas facility, the influence of the secondary chemistry could be quantified in a series of experiments. These results are taken into account in the molecular reaction chosen for the quantification of the individual aldehydes, so that the aldehydes in the present method are quantified, if possible, by reactions with the reagent ions NO^+ and OH^-.

All in all, several improvements in the production of test gases and their online analysis at the dynamic test gas facility could be achieved in the course of this work. The extended equipment for online monitoring of test gases now allows the selective quantitative analysis of more than 30 substances in a very short time. The developed methods can be regarded as equivalent to classical offline analysis with respect to recovery, limit of quantification, precision and correctness. Thus, the quality assurance of the test gases during method development and proficiency tests has been improved significantly.

With the introduction of the new pressure-based dosing system with combined vaporization and variable split ratio, precise test gas atmospheres of substances with high vapor pressure can be created. In the future the generation of the test gas for the aldehyde proficiency test can be done without methanol matrix and is state of the art in the production of dynamic test gases due to the use of precise pump technology.

Subsequent to this thesis, further work on the dosing system for substances with high vapor pressure should follow. For example, the change in concentration via the dosing rate should be carried out or the use of differently dimensioned capillary columns can be tested to extend the concentration range. The use of online measurement technology and the extension of the dosing technology opens up new possibilities to generate test gas atmospheres, which increase the method development possibilities at the dynamic test gas facility.

The SIFT-MS technique was found to be very useful for online analysis, nevertheless it is advisable that the reactions rates listed in the SIFT-compound library are checked and adjusted to meet the individual matrix criteria for e.g. humidity influences. Then this technique has the potential to meet the requirements for quality control of test gas atmospheres comparable to the established standard methods.

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8 Appendix

Appendix 1: List of all reactions for VOC determination in VOC proficiency test 2019 with SIFT-MS [39]

Compound	Reagent ion	Reaction rate k [cm^3 $molecule^{-1}$ s^{-1}]	Branching ratio (%)	Mass (m/z)	Product
1,2,4-Trimethylbenzene	H_3O^+	$2.4E^{-9}$	100	121	$C_9H_{12}\bullet H^+$
	NO^+	$1.9E^{-9}$	100	120	$C_9H_{12}^+$
	O_2^+	$2.0E^{-9}$	15	105	$C_8H_9^+$
	O_2^+	$2.0E^{-9}$	85	120	$C_9H_{12}^+$
Benzene	H_3O^+	$1.9E^{-9}$	100	79	$C_6H_6\bullet H^+$
	NO^+	$1.8E^{-9}$	76	78	$C_6H_6^+$
	NO^+	$1.8E^{-9}$	24	108	$NO\bullet C_6H_6^+$
	O_2^+	$1.6E^{-9}$	100	78	$C_6H_6^+$
Cumene	H_3O^+	$2.4E^{-9}$	10	43	$C_3H_7^+$
	H_3O^+	$2.4E^{-9}$	5	93	$C_7H_9^+$
	H_3O^+	$2.4E^{-9}$	10	105	$C_8H_9^+$
	H_3O^+	$2.4E^{-9}$	5	107	$C_8H_{11}^+$
	H_3O^+	$2.4E^{-9}$	70	121	$C_9H_{12}\bullet H^+$
	NO^+	$1.2E^{-9}$	15	43	$C_3H_7^+$
	NO^+	$1.2E^{-9}$	5	105	$C_8H_9^+$
	NO^+	$1.2E^{-9}$	5	106	$C_8H_{10}^+$
	NO^+	$1.2E^{-9}$	15	119	$C_9H_{11}^+$
	NO^+	$1.2E^{-9}$	60	120	$C_9H_{12}^+$
	O_2^+	$1.6E^{-9}$	25	43	$C_3H_7^+$
	O_2^+	$1.6E^{-9}$	65	105	$C_8H_9^+$
	O_2^+	$1.6E^{-9}$	5	106	$C_8H_{10}^+$
	O_2^+	$1.6E^{-9}$	5	120	$C_9H_{12}^+$
Ethyl acetate	H_3O^+	$2.9E^{-9}$	100	89	$CH_3COOC_2H_5\bullet H^+$
	H_3O^+	$2.9E^{-9}$		107	$CH_3COOC_2H_5\bullet H^+\bullet H_2O$
	NO^+	$2.7E^{-9}$	100	118	$NO^+\bullet CH_3COOC_2H_5$
	O_2^+	$1.8E^{-9}$	20	43	CH_3CO^+
	O_2^+	$1.8E^{-9}$	20	45	$C_2H_5O^+$
	O_2^+	$1.8E^{-9}$		63	$C_2H_5O^+\bullet H_2O$
	O_2^+	$1.8E^{-9}$		81	$C_2H_5O^+\bullet 2H_2O$
	O_2^+	$1.8E^{-9}$	40	61	$C_2H_5O_2^+$
	O_2^+	$1.8E^{-9}$		79	$C_2H_5O_2^+\bullet H_2O$
	O_2^+	$1.8E^{-9}$		97	$C_2H_5O_2^+\bullet 2H_2O$
	O_2^+	$1.8E^{-9}$	20	88	$C_4H_8O_2^+$
	O_2^+	$1.8E^{-9}$		106	$C_4H_8O_2^+\bullet H_2O$
Ethylbenzene	H_3O^+	$2.4E^{-9}$	100	107	$C_8H_{10}\bullet H^+$
	NO^+	$2.0E^{-9}$	100	106	$C_8H_{10}^+$
	O_2^+	$2.0E^{-9}$	70	91	$C_7H_7^+$
	O_2^+	$2.0E^{-9}$	30	106	$C_8H_{10}^+$
m-Xylene	H_3O^+	$2.3E^{-9}$	100	107	$C_8H_{10}\bullet H^+$
	NO^+	$1.9E^{-9}$	100	106	$C_8H_{10}^+$
	O_2^+	$1.9E^{-9}$	20	91	$C_7H_7^+$
	O_2^+	$1.9E^{-9}$	80	106	$C_8H_{10}^+$
Octane	H_3O^+	$9.0E^{-10}$	100	113	$C_8H_{17}^+$
	NO^+	$7.0E^{-10}$	80	113	$C_8H_{17}^+$
	O_2^+	$1.9E^{-9}$	30	114	$C_8H_{18}^+$
Toluene	H_3O^+	$2.2E^{-9}$	100	93	$C_7H_8\bullet H^+$
	NO^+	$1.7E^{-9}$	100	92	$C_7H_8^+$
	O_2^+	$1.8E^{-9}$	100	92	$C_7H_8^+$

Compound	Reagent ion	Reaction rate k [cm^3 $molecule^{-1}$ s^{-1}]	Branching ratio (%)	Mass (m/z)	Product
α-Pinene	H_3O^+	$2.6E^{-9}$	39	81	$C_6H_9^+$
	H_3O^+	$2.6E^{-9}$	61	137	$C_{10}H_{17}^+$
	NO^+	$2.3E^{-9}$	16	92	$C_7H_8^+$
	NO^+	$2.3E^{-9}$	7	93	$C_7H_9^+$
	NO^+	$2.3E^{-9}$	77	136	$C_{10}H_{16}^+$
	O_2^+	$2.1E^{-9}$	3	80	$C_6H_8^+$
	O_2^+	$2.1E^{-9}$	21	92	$C_7H_8^+$
	O_2^+	$2.1E^{-9}$	56	93	$C_7H_9^+$
	O_2^+	$2.1E^{-9}$	3	107	$C_8H_{11}^+$
	O_2^+	$2.1E^{-9}$	12	121	$C_9H_{13}^+$
	O_2^+	$2.1E^{-9}$	5	136	$C_{10}H_{16}^+$

Appendix 2: Calibration data 10-Point-calibration for online-VOC-analysis [72]. *Limit of quantification (LOQ) > lowest calibration level, restricted operation rang. ** Lower calibration levels not in the linear range

Compound	Calibration range [µg/m^3]	Calibration function	Correlation coefficient r	LOQ [µg/m^3]n	Coefficient of variation [%]
Butanone	5 - 254	$y = 0.322x - 0.129$	1.0000	3	0.53
Ethyl acetate	5 - 240	$y = 0.219x - 0.334$	1.0000	3	0.78
Benzene	5-262	$y = 0.592x + 0.233$	1.0000	3	0.47
2-Methoxyethanol *	5-254	$y = 0.182x - 1.108$	0.9999	9	1.41
Heptane	5-255	$y= 0.548x + 0.040$	1.0000	3	0.41
1-Methoxy-2-propanol *	10 - 241	$y = 0.247x - 0.689$	1.0000	8	0.71
1-Butanol	5-255	$y = 0.371x - 0.140$	1.0000	3	0.49
2-Ethoxyethanol *	19 - 243	$y = 0.361x + 3.376$	0.9973	15	5.61
4-Methyl-2-Pentanon	6-242	$y = 0.410x - 0.100$	0.9999	2	1.01
Toluene	5-265	$y = 0.586 + 0.139$	1.0000	3	0.52
1-Ethoxy-2-propanol *	10-242	$y = 0.286 - 1.306$	0.9999	6	1.3
Octane	5-256	$y = 0.545x + 0.347$	1.0000	3	0.56
Butylacetate	6-241	$y = 0.320x - 0.641$	1.0000	5	0.49
Ethylbenzene	5 - 254	$y = 0.576x + 0.138$	1.0000	3	0.46
m-Xylene	6-242	$y = 0.579x + 0.064$	1.0000	1	0.68
Nonane	5-255	$y = 0.546x - 0.028$	1.0000	3	0.44
α-Pinene	5-240	$y = 0.564x - 0.276$	1.0000	1	0.79
Cumene	5-257	$y = 0.572x + 0.105$	1.0000	4	0.43
2-Ethoxyethylacetate (I) **	40-241	$y = 0.146x - 5.779$	0.9945	84	7.01
2-Ethoxyethylacetate (II) *	91-196	$y = 0.121x - 7.657$	0.9994	86	1.34
Propylbenzene	5-259	$y = 0.577x - 0.141$	1.0000	3	0.39
Decane	5-256	$y = 0.538x +0.064$	1.0000	3	0.48
1,2,4-Trimethyl benzene	5-256	$y = 0.562x - 0.097$	1.0000	4	0.58
1,2,3-Trimethyl benzene	5-257	$y = 0.512x - 0.042$	1.0000	4	0.62

Appendix 3: Results of the calibration for determination of the limit of quantification. 6 levels (n=3). * 4-point-calibration due to restricted linear range [72]

Compound	Calibration range [µg/m^3]	Homogeneity of variance	Linearity (Mandel)	Limit of quantification [µg/m^3]
		$F_{2;2;0,01}$ = 99.00	$F_{1;3;0,01}$ = 34.12	$t_{4;0.01}$ = 5.598; k = 3
Butanone	2.5 – 25	Yes	yes	3
Ethyl acetate	2.5 – 25	Yes	yes	3
Benzene	2.5 – 25	Yes	yes	3
2-Methoxyethanol	2.5 – 25	up to 20.5 µg/m^3	yes	9
Heptane	2.5 – 25	yes	yes	3
1-Methoxy-2-propanol	2.5 – 25	up to 16 µg/m^3	yes	8
1-Butanol	2.5 – 25	yes	yes	3
2-Ethoxyethanol	2.5 – 25	yes	yes	15
4-Methyl-2-Pentanon	2.5 – 25	yes	yes	2
Toluene	2.5 – 25	yes	yes	3
1-Ethoxy-2-propanol	2.5 – 25	up to 16 µg/m^3	yes	6
Octane	2.5 – 25	yes	yes	3
Butyl acetate	2.5 – 25	yes	yes	5
Ethylbenzene	2.5 – 25	yes	yes	3
m-Xylene	2.5 – 25	yes	yes	1
Nonane	2.5 – 25	yes	yes	3
α-Pinene	2.5 – 25	yes	yes	1
Cumene	2.5 – 25	yes	yes	4
2-Ethoxyethylacetate *	20 – 200	yes	yes	86
Propylbenzene	2.5 – 25	yes	yes	3
Decane	2.5 – 25	yes	yes	3
1,2,4-Trimethyl benzene	2.5 – 25	yes	yes	4
1,2,3-Trimethyl benzene	2.5 - 25	yes	yes	4

Appendix 4: Results of the verification of the online-measurements with independent offline-TD-GC-MS analysis. [72]

Compound	Calculated concentration [µg/m^3]	Results Online- GC (n=3) [%]						Results Offline-GC (n = 2) [%]		
		Relative standard deviation			Recovery rate			Recovery rate		
		Mean	Min	Max	Mean	Min	Max	Mean	Min	Max
Butanone *	185.4	1.1	0.2	1.9	96	94	100	105	103	109
Ethyl acetate*	10.3	3.9	1.4	7.0	128	126	133	102	100	105
Benzene	109.2	1.2	0.1	2.1	97	95	100	103	100	105
2-Methoxyethanol * +	63.0	4.2	0.9	8.2	48	45	52	108	106	112
Heptane*	97.8	1.1	0.2	2.2	106	104	109	109	107	111
1-Methoxy-2-propanol +	167.0	3.0	0.7	4.9	96	94	99	96	93	99
1-Butanol	165.3	2.9	2.3	3.7	104	102	108	95	91	98
2-Ethoxyethanol **	48.2	5.3	1.9	8.0	119	112	127	101	98	104
4-Methyl-2-pentanone	183.2	1.5	0.7	2.5	98	96	100	101	99	103
Toluene	70.5	1.3	0.4	2.2	98	97	101	99	97	102
1-Ethoxy-2-propanol + ++	17.2	1.2	0.4	2.1	101	100	103	104	101	106
Octane++	109.1	1.3	0.4	2.2	101	100	103	103	101	105
Butylacetate	90.9	1.8	1.3	2.3	101	99	102	102	100	104
Ethylbenzene	133.1	1.9	1.3	2.7	99	97	101	97	95	100
m-Xylene*	162.4	2.0	1.5	2.8	98	97	100	97	96	99
Nonane*	13.7	1.7	1.2	2.3	99	95	106	117	114	121
α-Pinene	145.8	1.6	0.9	2.4	98	97	100	103	101	105
Cumene++	142.8	2.4	1.7	2.8	103	101	104	97	95	100
2-Ethoxyethylacetate ++ x	72.3	2.2	1.5	2.6	103	101	104	111	108	114
Propylbenzene	147.5	3.0	2.2	4.2	99	97	102	94	91	97
Decane	94.6	2.0	1.3	2.5	100	98	104	100	97	102
1,2,4-Trimethylbenzene	102.1	3.7	2.6	6.2	100	96	104	96	92	100
1,2,3- Trimethylbenzene	85.0	4.1	1.6	6.1	99	96	102	92	88	98

* Co-eluting in online-GC

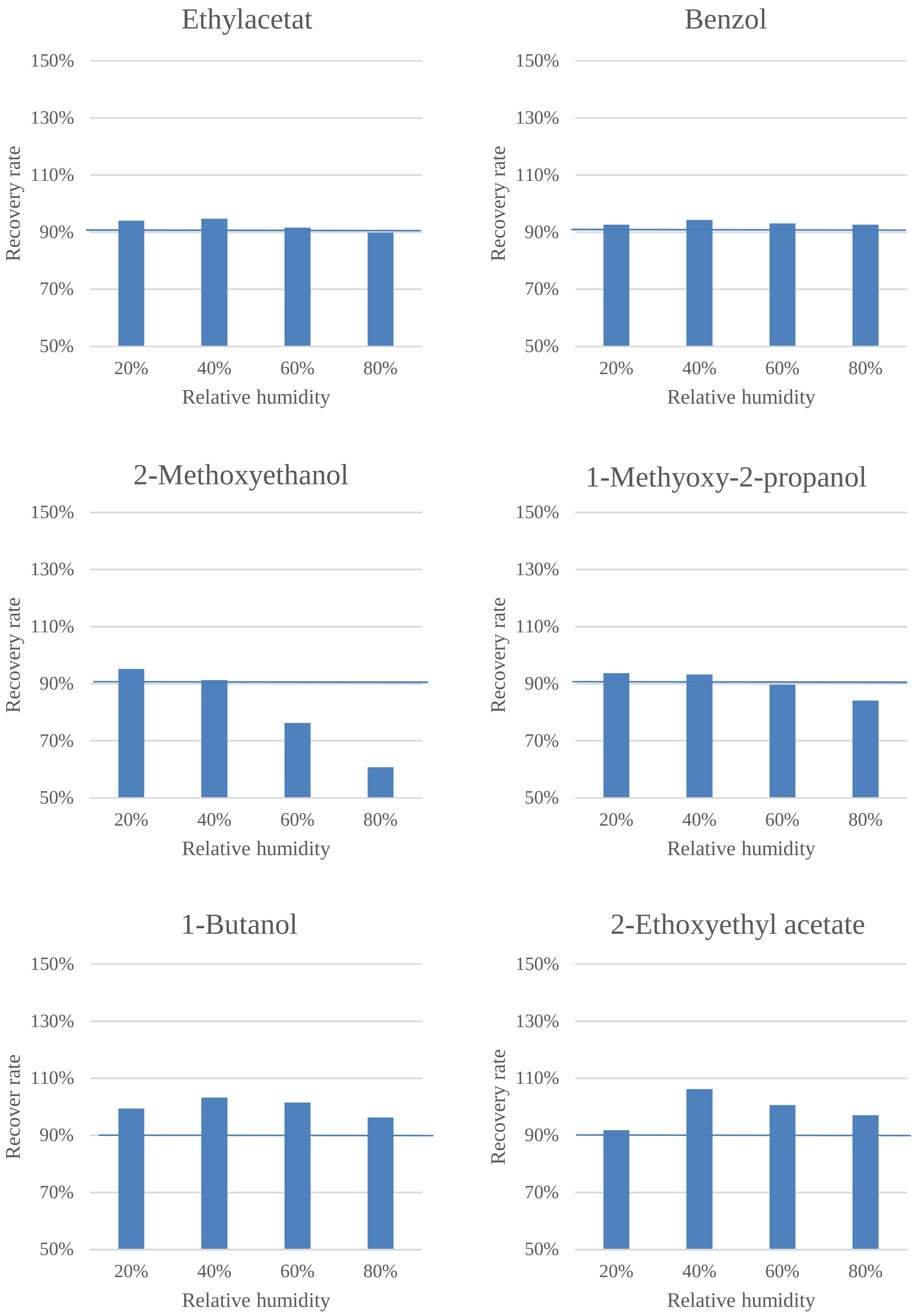
** 8-Point-Calibration, 5 and 10 µg/m^3 < Limit of Quantification

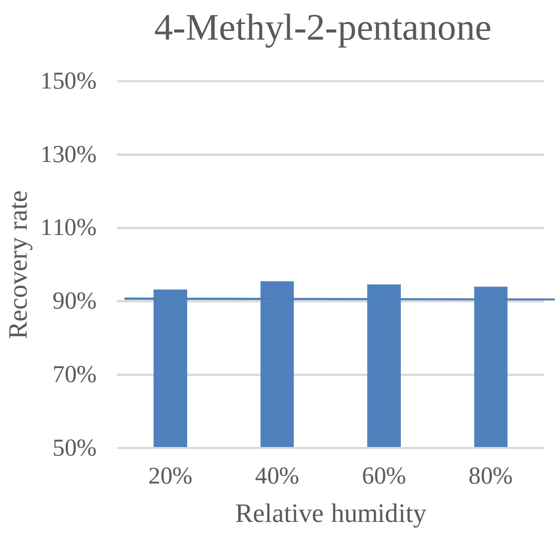
\+ 9-Punkt-Kalibrierung, 5 µg/m^3 < Limit of Quantification

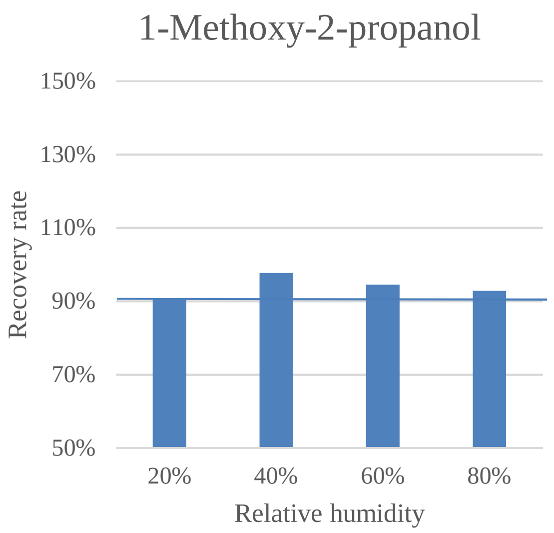
\++ Co-eluting in online-GC, combined recovery in online-GC method based on expected sum peak area

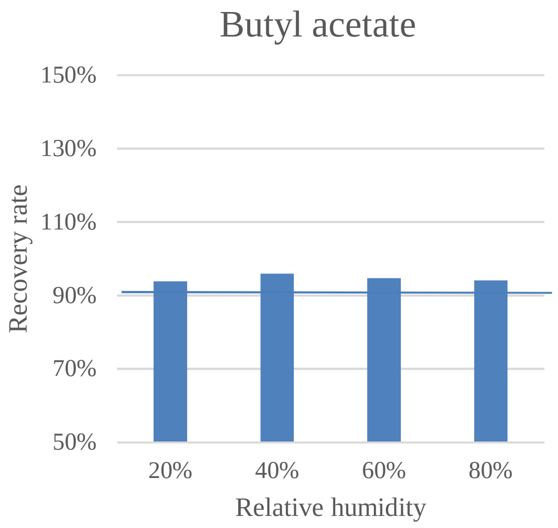
x c < Limit of Quantification, determined with 4-point calibration

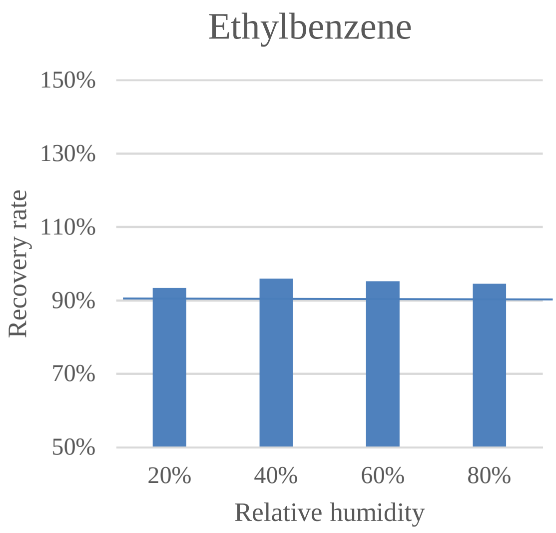
Appendix 5: Recovery in the analysis of a 90 µg/m³ test gas with different humidity conditions; error indicators show the standard deviation of the triple determination; blue line: lower limit of acceptance of recovery 90 %, red line: upper limit of acceptance 110 %. [72]

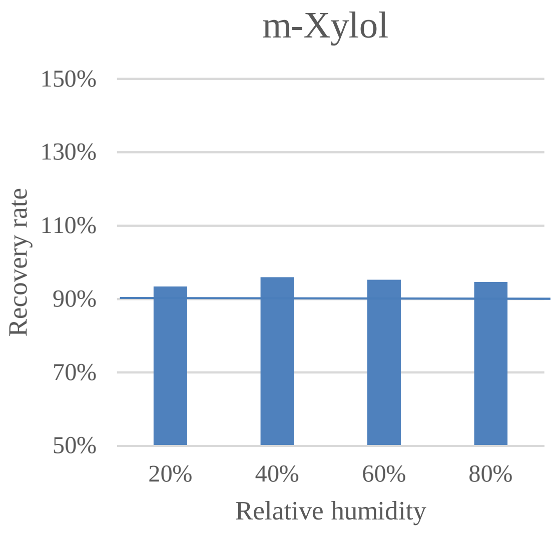


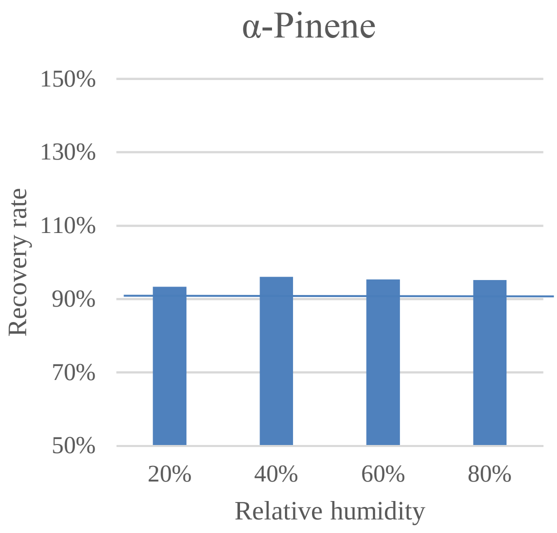

4-Methyl-2-pentanone
150%
130%
110%
90%
70%
50%
Recovery rate
20%
40%
60%
80%
Relative humidity

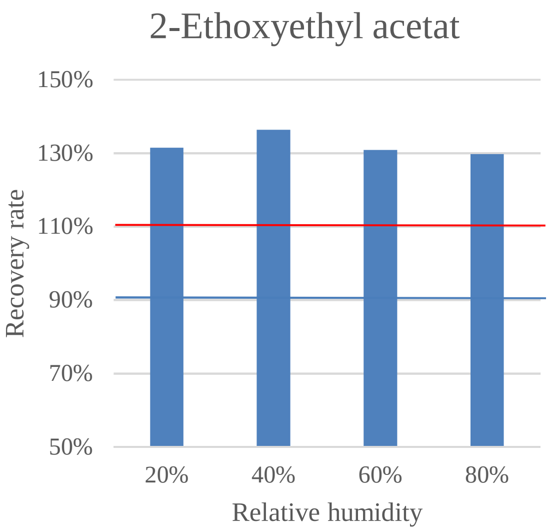

1-Methoxy-2-propanol
150%
130%
110%
90%
70%
50%
Recovery rate
20%
40%
60%
80%
Relative humidity

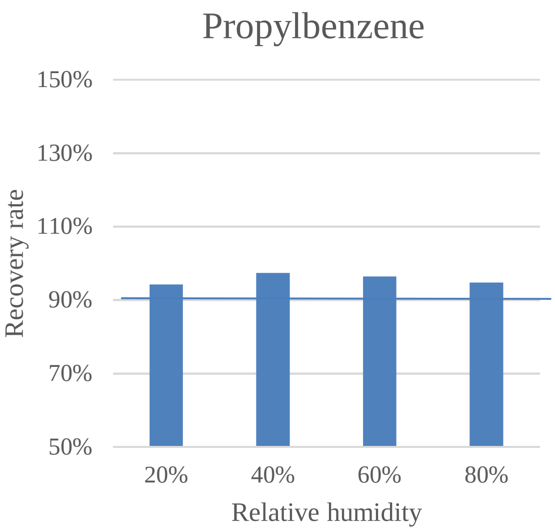

Butyl acetate
150%
130%
110%
90%
70%
50%
Recovery rate
20%
40%
60%
80%
Relative humidity

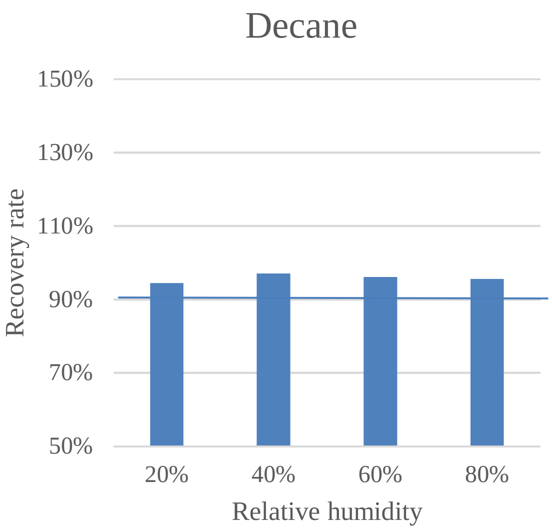

Ethylbenzene
150%
130%
110%
90%
70%
50%
Recovery rate
20%
40%
60%
80%
Relative humidity

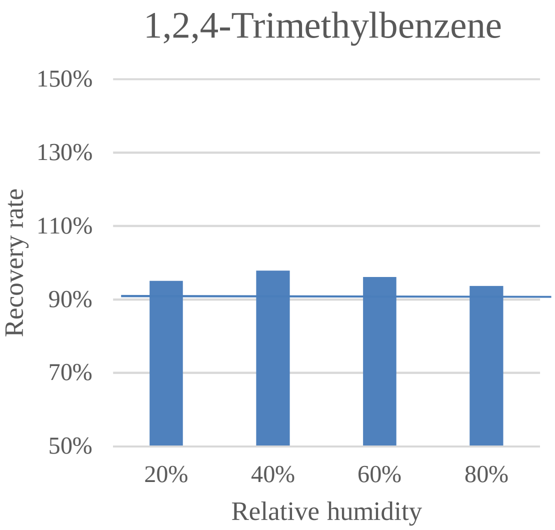

m-Xylol
150%
130%
110%
90%
70%
50%
Recovery rate
20%
40%
60%
80%
Relative humidity

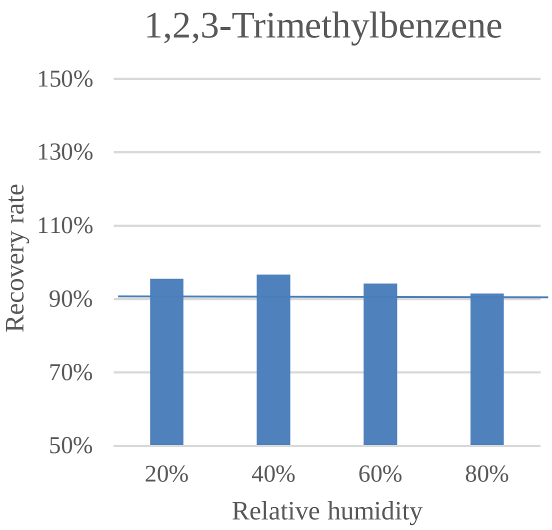

α-Pinene
150%
130%
110%
90%
70%
50%
Recovery rate
20%
40%
60%
80%
Relative humidity


2-Ethoxyethyl acetat


Propylbenzene


Decane


1,2,4-Trimethylbenzene


1,2,3-Trimethylbenzene

Appendix 6-1: Calibration summary for organic solvents proficiency test 2018.

	Calibration level	Calculated concentration [mg/m³]	Average area (n=3)	Relative standard deviation [%]	Slope	Intercept	Correlation coefficient r	Limit of quantification [mg/m³]	Standard deviation of process
n-Hexane	1	5.9	0.32	0.31	0.053	0.004	1.0000	0.82	0.081
	2	11.8	0.63	1.01					
	3	29.4	1.57	0.81					
	4	44.1	2.36	0.44					
	5	58.8	3.14	0.62					
n-Heptane	1	59.0	3.10	0.26	0.054	-0.066	1.0000	3.1	0.298
	2	118	6.27	0.65					
	3	295	15.72	0.62					
	4	442	23.62	0.31					
	5	590	31.56	0.61					
Cyclohexane	1	14.0	0.79	2.54	0.057	-0.012	0.9999	1.0	0.098
	2	28.1	1.58	0.95					
	3	70.1	3.95	0.62					
	4	105	5.95	0.25					
	5	140	7.94	0.64					
Methylcyclo hexane	1	11.5	0.65	0.38	0.055	0.007	0.9999	1.1	0.105
	2	23.1	1.28	1.90					
	3	57.6	3.19	0.43					
	4	86.4	4.78	0.53					
	5	115	6.38	0.55					
n-Octane	1	52.2	2.74	0.31	0.054	-0.090	1.0000	4.2	0.411
	2	105	5.56	0.79					
	3	261	14.00	0.90					
	4	392	21.04	0.32					
	5	522	28.15	0.60					

Appendix 6-2: Calibration summary for organic solvents proficiency test 2018.

	Calibration level	Calculated concentration [mg/m^3]	Average area (n=3)	Relative standard deviation [%]	Slope	Intercept	Correlation coefficient r	Limit of quantification [mg/m^3]	Standard deviation of process
Ethyl acetate	1	50.7	0.86	2.26	0.025	-0.254	0.9996	58.8	6.23
	2	101	2.25	9.36					
	3	253	6.11	1.25					
	4	380	9.17	0.68					
	5	507	12.04	1.90					
n-Decane	1	7.1	0.36	0.97	0.052	-0.007	1.0000	1.4	0.134
	2	14.2	0.74	1.41					
	3	35.5	1.84	0.52					
	4	53.3	2.76	0.59					
	5	71.1	3.70	0.73					
2-Butanol	1	16.6	0.48	2.00	0.037	-0.188	0.9999	9.7	0.988
	2	33.1	1.01	0.96					
	3	82.7	2.89	0.62					
	4	124	4.46	0.76					
	5	166	6.00	0.98					
Toluene	1	12.1	0.72	0.48	0.062	0.035	0.9999	8.2	0.841
	2	24.2	1.55	0.94					
	3	60.3	3.81	0.77					
	4	90.5	5.62	0.63					
	5	121	7.44	0.62					
1-Propanol	1	78.8	2.39	1.51	0.038	-0.540	0.9999	37.6	3.79
	2	158	5.47	0.91					
	3	394	14.74	0.77					
	4	591	22.15	0.88					
	5	787	29.54	0.92					

Appendix 6-3: Calibration summary for organic solvents proficiency test 2018.

	Calibration level	Calculated concentration [mg/m³]	Average area (n=3)	Relative standard deviation [%]	Slope	Intercept	Correlation coefficient r	Limit of quantification [mg/m³]	Standard deviation of process
2-Methyl-1-propanol	1	22.8	0.77	1.56	0.045	-0.254	1.0000	4.0	0.39
	2	45.6	1.76	1.13					
	3	114	4.85	0.91					
	4	171	7.37	1.23					
	5	228	9.91	1.04					
Ethylbenzene	1	7.0	0.42	3.25	0.057	0.010	1.0000	0.92	0.09
	2	14.1	0.81	0.76					
	3	35.1	2.00	0.68					
	4	52.7	3.00	0.74					
	5	70.3	4.01	0.88					
p-Xylene	1	20.3	1.16	0.00	0.058	0.001	1.0000	3.4	0.336
	2	40.6	2.35	0.75					
	3	101	5.83	0.73					
	4	152	8.73	0.51					
	5	203	11.7	0.85					
1-Butanol	1	12.6	0.34	2.98	0.040	-0.209	0.9997	12.8	1.341
	2	25.1	0.78	3.82					
	3	62.8	2.21	0.90					
	4	94.2	3.53	0.85					
	5	126	4.82	1.28					
Cumene	1	3.1	0.19	1.03	0.056	0.018	0.9999	1.5	0.149
	2	6.1	0.36	2.39					
	3	15.3	0.87	0.84					
	4	23.0	1.30	1.15					
	5	30.6	1.74	1.23					

Appendix 7: Summary of quality control samples (Q1-Q3) for proficiency test organic solvents 2018.

		n-Decane	Cumene	p-Xylene	Ethylbenzene	n-Octane	1-Butanol	Toluene	2-Methyl-1-propanol	Methylcyclohexane	2-Butanol	n-Heptane	1-Propanol	Cyclohexane	Ethyl acetate	n-Hexane
Q1	Calc. conc. [mg/m³]	10.4	4.6	30.9	10.3	77.5	19.2	18.2	34	17.6	25.8	88.3	117	21.5	75.3	10.5
	Average conc. (n=6) [mg/m³]	10.5	4.6	30.8	10.3	77.3	19.6	17.6	32.7	17.4	25.3	87.8	111	21.4	69.7	10.3
	Standard deviation [mg/m³]	0.2	0.1	0.5	0.2	0.7	0.3	0.5	0.8	0.3	0.4	0.9	3.5	0.5	3.2	0.2
	Relative standard deviation [%]	2.2	1.8	1.5	1.8	0.9	1.7	2.7	2.4	1.5	1.6	1	3.2	2.2	4.6	1.7
	Recovery rate [%]	**101**	**102**	**100**	**100**	**100**	**102**	**97**	**96**	**99**	**98**	**99**	**95**	**99**	**93**	**99**
Q2	Calc. conc. [mg/m³]	41.5	18.2	123	41.1	310	76.8	72.8	136	70.3	103	353	469	85.9	301	41.9
	Average conc. (n=6) [mg/m³]	41.4	18.2	123	41.2	310	78.3	73.7	138	70.8	104	353	472	85.8	318	41.6
	Standard deviation [mg/m³]	0.2	0.2	0.6	0.3	2.1	0.6	0.5	1.2	0.4	0.9	2.1	3.5	0.6	0.6	0.2
	Relative standard deviation [%]	0.6	1.3	0.5	0.6	0.7	0.7	0.6	0.8	0.5	0.8	0.6	0.7	0.7	0.2	0.6
	Recovery rate [%]	**100**	**100**	**100**	**100**	**100**	**102**	**101**	**101**	**101**	**101**	**100**	**101**	**100**	**106**	**99**
Q3	Calc. conc. [mg/m³]	58.8	25.8	175	58.3	439	109	103	192	99.6	146	500	664	122	427	59.3
	Average conc. (n=6) [mg/m³]	58.1	25.5	173	58.1	434	110	102	191	98.7	145	495	653	120	433	58.4
	Standard deviation [mg/m³]	0.8	0.5	2.5	0.9	5.8	1.5	2	3.1	1.7	2.7	6.9	12.1	1.8	7.6	0.7
	Relative standard deviation [%]	**1.4**	**1.9**	**1.4**	**1.5**	**1.3**	**1.4**	**2.0**	**1.6**	**1.7**	**1.8**	**1.4**	**1.9**	**1.5**	**1.8**	**1.3**
	Recovery rate [%]	**99**	**99**	**99**	**100**	**99**	**101**	**98**	**99**	**99**	**100**	**99**	**98**	**99**	**102**	**98**

Appendix 8-1: Calibration summary proficiency test for organic solvents 2019 – online-GC calibration.

	Calibration Level	Calculated concentration [mg/m³]	Average area (n=3)	Relative standard deviation [%]	Slope	Intercept	correlation coefficient	Limit of detection [mg/m³]	Limit of quantification [mg/m³]	Standard deviation of process
n-Decane	1	5.55	0.32	2.84	0.054	0.017	1.0000	0.174	0.704	0.074
	2	30.6	1.66	0.56						
	3	61.1	3.32	0.28						
	4	90.3	4.88	0.39						
	5	118	6.39	0.52						
Cumene	1	0.86	0.06	11	0.058	0.008	1.0000	0.108	0.430	0.046
	2	4.72	0.29	3.32						
	3	9.45	0.56	1.02						
	4	14.0	0.82	0.52						
	5	18.3	1.08	0.74						
x-Xylene	1	5.45	0.37	1.30	0.060	0.044	1.0000	0.267	1.07	0.114
	2	30.0	1.83	0.17						
	3	60.0	3.62	0.20						
	4	88.6	5.31	0.21						
	5	116	6.95	0.29						
Methyl cyclohexane	1	9.76	0.56	0.03	0.056	-0.002	1.0000	0.519	2.09	0.221
	2	53.7	3.00	0.09						
	3	107	6.02	0.08						
	4	159	8.89	0.35						
	5	207	11.65	0.32						
2-Butanol	1	2.98	0.11	6.88	0.040	-0.101	0.9965	5.47	17.7	2.33
	2	16.4	0.49	1.88						
	3	32.8	1.10	0.66						
	4	48.4	1.85	0.44						
	5	63.3	2.47	0.59						

Appendix 8-2: Calibration summary proficiency test for organic solvents 2019 – online-GC calibration.

	Calibration Level	Calculated concentration [mg/m³]	Average Area (n=3)	Relative standard deviation [%]	Slope	Intercept	correlation coefficient	Limit of detection [mg/m³]	Limit of quantification [mg/m³]	Standard deviation of process
1-Propanol	1	12.6	0.40	1.56	0.039	-0.289	0.9990	12.4	43.7	5.29
	2	69.2	2.28	1.15						
	3	139	4.84	0.28						
	4	205	7.65	0.75						
	5	268	10.21	0.75						
2-Propanol	1	10.4	0.29	4.62	0.035	-0.290	0.9984	13.0	44.4	5.53
	2	57.2	1.51	0.75						
	3	114	3.67	5.03						
	4	169	5.60	3.14						
	5	221	7.56	0.40						
Cyclohexane	1	10.2	0.58	1.34	0.056	-0.013	1.0000	0.864	3.45	0.368
	2	56.1	3.14	0.05						
	3	112	6.31	0.15						
	4	166	9.33	0.10						
	5	217	12.25	0.25						
Ethyl acetate	1	16.8	0.35	2.55	0.030	-0.397	0.9964	31.3	101	13.3
	2	92.5	1.79	2.60						
	3	185	5.35	0.39						
	4	273	7.81	0.29						
	5	358	10.05	0.08						
1,2,4-Trimethyl benzene	1	8.6	0.67	1.10	0.063	0.283	0.9996	5.33	19.7	2.27
	2	47.0	3.37	2.30						
	3	94.0	6.35	1.53						
	4	139	9.02	1.31						
	5	182	11.63	0.90						

Appendix 8-3: Calibration summary proficiency test for organic solvents 2019 – online-GC calibration.

	Calibration Level	Calculated concentration [mg/m³]	Average Area (n=3)	Relative standard deviation [%]	Slope	Intercept	Correlation coefficient r	Limit of detection [mg/m³]	Limit of quantification [mg/m³]	Standard deviation of process
n-Nonane	1	16.9	0.91	0.93	0.054	-0.024	1.0000	1.294	5.184	0.552
	2	93.2	5.07	1.04						
	3	186	10.16	0.57						
	4	275	14.95	0.68						
	5	360	19.67	0.77						
Ethylbenzene	1	6.04	0.37	0.13	0.059	0.020	1.0000	0.586	2.34	0.250
	2	33.2	1.98	0.74						
	3	66.5	3.94	0.73						
	4	98.2	5.78	0.75						
	5	128	7.58	0.38						
1-Butanol	1	6.54	0.15	0.82	0.040	-0.224	0.9992	5.813	20.716	2.48
	2	36.0	1.16	3.63						
	3	71.9	2.58	0.88						
	4	106	4.03	0.84						
	5	139	5.44	0.87						
Toluene	1	3.79	0.24	2.01	0.060	0.009	1.0000	0.223	0.897	0.095
	2	20.8	1.25	0.47						
	3	41.7	2.51	0.93						
	4	61.6	3.67	0.75						
	5	80.6	4.82	0.46						
2-Methyl-1-Propanol	1	8.30	0.28	1.88	0.046	-0.278	0.9990	8.127	28.648	3.47
	2	45.6	1.68	0.68						
	3	91.3	3.85	0.99						
	4	135	5.89	0.59						
	5	176	8.00	1.11						

Appendix 8-4: Calibration summary proficiency test for organic solvents 2019 – online-GC calibration.

	Calibration Level	Calculated concentration [mg/m³]	Average Area (n=3)	Relative standard deviation [%]	Slope	Intercept	Correlation coefficient r	Limit of detection [mg/m³]	Limit of quantification [mg/m³]	Standard deviation of process
Ethanol	1	22.6	0.55	3.63	0.031	-0.347	0.9994	16.8	60.9	7.149
	2	124	3.23	4.21						
	3	248	7.48	0.76						
	4	367	11.18	1.35						
	5	480	14.68	1.13						
n-Hexane	1	1.88	0.10	3.59	0.054	0.000	1.0000	0.195	0.777	0.083
	2	10.4	0.55	0.64						
	3	20.7	1.12	0.60						
	4	30.6	1.65	0.51						
	5	40.0	2.16	0.31						

Appendix 9: Summary of quality control samples for proficiency test organic solvents 2019.

		n-Decane	Cumene	m-Xylene	Methyl-cyclohexane	2-Butanol	1-Propanol	2-Propanol	Cyclohexane	Ethyl acetate	1,2,4-TMB	n-Nonane	Ethylbenzene	1-Butanol	Toluene	2-Methyl-1-propanol	Ethanol	n-Hexane
Q1	Calc. conc. [mg/m³]	13.9	2.2	13.7	23.3	8.10	31.6	26.0	25.6	42.2	21.5	42.3	15.1	16.0	9.5	20.7	56.6	4.6
	Average conc. (n=6) [mg/m³]	14.1	2.3	14.1	23.2	8.00	30.7	25.4	25.6	37.5	20.7	41.7	15.0	14.1	9.5	19.7	50.5	4.7
	Standard deviation [mg/m³]	0.56	0.16	0.56	0.94	0.55	1.35	0.99	1.01	1.61	0.36	0.51	0.13	0.5	0.14	0.35	1.41	0.19
	Relative standard deviation [%]	4.0	6.7	4.0	4.1	6.9	4.4	3.9	3.9	4.3	1.7	1.2	0.9	3.5	1.5	1.8	2.8	4.0
	Recovery rate [%]	**101**	**108**	**103**	**99**	**99**	**97**	**98**	**100**	**89**	**96**	**99**	**99**	**88**	**100**	**95**	**89**	**101**
Q2	Calc. conc. [mg/m³]	41.8	6.5	41.1	70.0	24.4	94.8	78.1	76.9	127	64.4	127	45.3	47.9	28.6	62.2	170	13.9
	Average conc. (n=2) [mg/m³]	42.2	6.6	42.0	70.4	21.3	84.4	65.9	77.4	141	65.1	125	44.7	43.7	28.2	57.4	162	13.9
	Standard deviation [mg/m³]	0.18	0.13	0.18	0.38	0.25	2.76	0.32	0.43	1.03	0.95	0.77	0.37	1.1	0.13	1.4	6.24	0.08
	Relative standard deviation [%]	0.4	1.9	0.4	0.5	1.2	3.3	0.5	0.6	0.7	1.5	0.6	0.8	2.5	0.4	2.4	3.9	0.6
	Recovery rate [%]	**101**	**101**	**102**	**101**	**87**	**89**	**84**	**101**	**111**	**101**	**98**	**99**	**91**	**99**	**92**	**95**	**100**
Q3	Calc. conc. [mg/m³]	97.5	15.1	96.0	163	57.0	221	182	179	295	150	296	106	112	66.7	145	396	32.5
	Average conc. (n=6) [mg/m³]	98.7	15.6	97.9	166	59.4	228	191	181	313	148	292	104	111	66.0	144	386	32.3
	Standard deviation [mg/m³]	0.99	0.17	0.8	1.09	0.39	2.27	2.06	0.98	2.73	1.83	2.07	0.69	1.32	0.36	1.4	12.5	0.23
	Relative standard deviation[%]	1.0	1.1	0.8	0.7	0.7	1.0	1.1	0.5	0.9	1.2	0.7	0.7	1.2	0.5	1.0	3.2	0.7
	Recovery rate [%]	**101**	**103**	**102**	**101**	**104**	**103**	**105**	**101**	**106**	**98**	**99**	**99**	**99**	**99**	**99**	**97**	**99**

Appendix 10-1: Results of online- and offline-GC measurements of the proficiency test organic solvents 2018 (Test gas mixture 2 and 3).

TGM 2	Calculated concentration [mg/m³]	Method	Min. concentration [mg/m³]	Max. concentration [mg/m³]	Average concentration [mg/m³]	Standard deviation [mg/m³]	Relative standard deviation [%]	Recovery rate [%]
Cumene	15.2	**Online-GC (n=25)**	14.7	15.5	15.1	0.20	1.3	**99**
		Offline-GC (n=10)	15.4	15.9	15.7	0.16	1.1	**103**
Ethyl acetate	253	**Online-GC (n=25)**	266	283	278	3.76	1.4	**110**
		Offline-GC (n=10)	263	276	270	4.13	1.5	**107**
Ethylbenzene	35.0	**Online-GC (n=25)**	33.8	35.4	34.7	0.35	1.0	**99**
		Offline-GC (n=10)	34.6	35.4	35.1	0.27	0.8	**100**
Toluene	60.7	**Online-GC (n=25)**	55.0	57.8	56.5	0.51	0.9	**93**
		Offline-GC (n=10)	60.0	61.9	61.0	0.53	0.9	**101**
p-Xylene	102	**Online-GC (n=25)**	98.2	103	101	0.83	0.8	**99**
		Offline-GC (n=10)	101	105	103	1.52	1.5	**101**

Appendix 10-2: Results of online- and offline-GC measurements of the proficiency test organic solvents 2018 (Test gas mixture 2 and 3).

TGM 3	Calculated concentration [mg/m^3]	Method	Min. concentration [mg/m^3]	Max. concentration [mg/m^3]	Average concentration [mg/m^3]	Standard deviation [mg/m^3]	Relative standard deviation [%]	Recovery rate [%]
1-Butanol	62.3	**Online-GC (n=25)**	61.2	65.6	63.0	1.14	1.8	**101**
		Offline-GC (n=10)	58.5	60.0	59.4	0.54	0.9	**95**
2-Butanol	80.4	**Online-GC (n=25)**	71.5	88.2	77.9	6.31	8.1	**97**
		Offline-GC (n=10)	83.7	87.0	85.8	1.19	1.4	**107**
2-Methyl-1-propanol	115	**Online-GC (n=25)**	112	116	114	1.30	1.1	**99**
		Offline-GC (n=10)	116	119	118	1.33	1.1	**103**
1-Propanol	395	**Online-GC (n=25)**	386	398	394	2.81	0.7	**100**
		Offline-GC (n=10)	393	410	404	5.91	1.5	**102**

Appendix 11-1: Results of online- and offline-GC measurements of the proficiency test organic solvents 2019 (Test gas mixture 1-3).

TGM 1	Calculated concentration [mg/m³]	Method	Min. concentration [mg/m³]	Max. concentration [mg/m³]	Average concentration [mg/m³]	Standard deviation [mg/m³]	Relative standard deviation [%]	Recovery rate [%]
Cumene	9.5	**Online-GC (n=24)**	9.31	9.8	9.5	0.14	1.5	**100**
		Offline-GC (n=9)	8.99	9.2	9.1	0.07	0.8	**96**
Ethyl acetate	186	**Online-GC (n=24)**	143	152	147	2.17	1.5	**79**
		Offline-GC (n=9)	187	189	188	0.83	0.4	**101**
Ethylbenzene	67.4	**Online-GC (n=24)**	66.5	68.3	67.5	0.47	0.7	**100**
		Offline-GC (n=9)	65.9	67.3	66.5	0.48	0.7	**99**
Toluene	44.9	**Online-GC (n=24)**	44.0	45.4	45.0	0.38	0.9	**100**
		Offline-GC (n=9)	45.2	46.4	45.7	0.38	0.8	**102**
m-Xylene	62.2	**Online-GC (n=24)**	61.5	63.3	62.3	0.52	0.8	**100**
		Offline-GC (n=9)	62.7	64.0	63.2	0.45	0.7	**102**
1,2,4-Trimethyl benzene	93.5	**Online-GC (n=24)**	91.8	94.4	93.3	0.72	0.8	**100**
		Offline-GC (n=9)	98.2	101	99.3	0.73	0.7	**106**

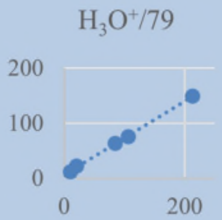
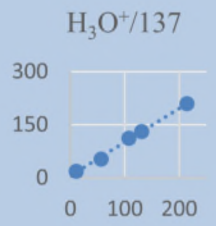
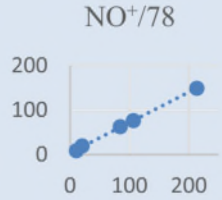
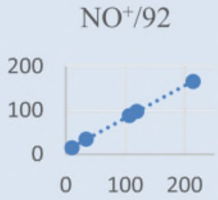
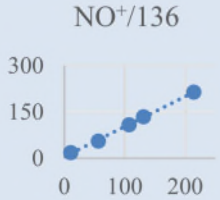
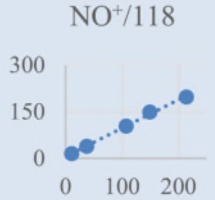
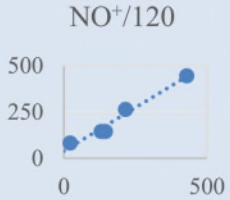
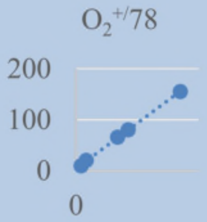
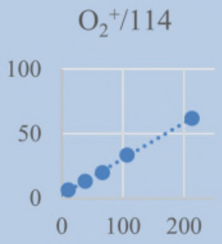
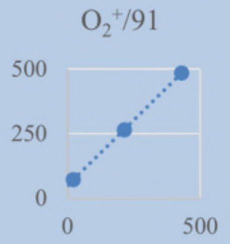
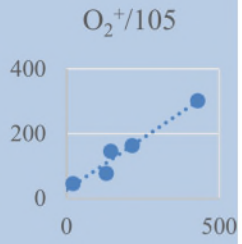
Appendix 11-2: Results of online- and offline-GC measurements of the proficiency test organic solvents 2019 (Test gas mixture 1-3).

TGM 2	Calculated concentration [mg/m³]	Method	Min. concentration [mg/m³]	Max. concentration [mg/m³]	Average concentration [mg/m³]	Standard deviation [mg/m³]	Relative standard deviation [%]	Recovery rate [%]
Cyclohexane	114	**Online-GC (n=21)**	110	114	112	0.75	0.7	**98**
		Offline-GC (n=10)	112	115	114	0.66	0.6	**100**
n-Decane	66.3	**Online-GC (n=21)**	65.0	66.6	65.6	0.42	0.6	**99**
		Offline-GC (n=10)	61.7	63.5	62.8	0.54	0.9	**95**
n-Hexane	21.7	**Online-GC (n=21)**	21.6	22.3	21.8	0.17	0.8	**101**
		Offline-GC (n=10)	19.6	20.1	19.9	0.15	0.8	**92**
Methyl cyclohexane	105	**Online-GC (n=21)**	102	105	104	0.58	0.6	**98**
		Offline-GC (n=10)	103	106	104	0.76	0.7	**99**
n-Nonane	249	**Online-GC (n=21)**	244	250	247	1.49	0.6	**99**
		Offline-GC (n=10)	251	258	255	1.98	0.8	**102**

Appendix 11-3: Results of online- and offline-GC measurements of the proficiency test organic solvents 2019 (Test gas mixture 1-3).

TGM 3	Calculated concentration [mg/m³]	Method	Min. concentration [mg/m³]	Max. concentration [mg/m³]	Average concentration [mg/m³]	Standard deviation [mg/m³]	Relative standard deviation [%]	Recovery rate [%]
1-Butanol	69.9	**Online-GC (n=22)**	68.1	72.1	70.3	1.03	1.5	**101**
		Offline-GC (n=10)	70.6	72.7	71.5	0.69	1.0	**102**
2-Butanol	32.9	**Online-GC (n=22)**	32.6	34.9	33.9	0.56	1.7	**103**
		Offline-GC (n=10)	34.4	35.5	34.9	0.36	1.0	**106**
2-Methyl-1-propanol	92.5	**Online-GC (n=22)**	89.9	93.1	91.4	0.84	0.9	**99**
		Offline-GC (n=10)	91.5	94.3	92.7	0.90	1.0	**100**
Ethanol	253	**Online-GC (n=22)**	273	280	276	1.65	0.6	**109**
		Offline-GC (n=10)	248	256	252	3.32	1.3	**100**
1-Propanol	143	**Online-GC (n=22)**	145	150	147	1.29	0.9	**103**
		Offline-GC (n=10)	141	146	144	1.64	1.1	**101**
2-Propanol	116	**Online-GC (n=22)**	97.1	98.8	97.9	0.45	0.5	**85**
		Offline-GC (n=10)	115	119	117	1.19	1.0	**101**

Appendix 12: Calibration functions for the determination of VOCs during the proficiency test using SIFT-MS.

Benzene	Toluene	α-Pinene	Ethylacetate	Octane	p-Xylene+ Ethylbenzene	1,2,4-Trimethylbenzene + Cumene
 y = 0.6696x + 5.808 R² = 0.999		 y = 0.9511x + 5.7685 R² = 0.9968				
 y = 0.6844x + 3.7723 R² = 0.9991	 y = 0.7401x + 8.2101 R² = 0.9997	 y = 0.9734x + 5.3368 R² = 0.9987	 y = 0.9121x + 6.0498 R² = 0.9971			 y = 0.936x + 40.024 R² = 0.9722
 y = 0.7118x + 4.2684 R² = 0.9994				 y = 0.2781x + 2.687 R² = 0.9984	 y = 1.0129x + 48.905 R² = 0.9999	 y = 0.6387x + 25.839 R² = 0.9541

Appendix 13-1: SIFT-MS reported concentrations per product ion and related results of offline-HPLC analysis and calculated concentration for aldehyde calibration.

Calibration Level	Calculated concentration [mg/m³]	result HPLC [mg/m³]	SIFT reported concentration per product ion [mg/m³]					
			$C_2H_2O^-$ [42] / O^- / acetaldehyde	$C_2H_3O^+$ [43] / O_2^+ / acetaldehyde	$C_2H_3O^-$ [43] / O^- / acetaldehyde	$C_2H_3O^-$ [43] / OH^- / acetaldehyde	$C_2H_5O^+$ [45] / H_3O^+ / acetaldehyde	CH_3CO^+ [43] / NO^+ / acetaldehyde
1	0.062	0.080	0.055	0.126	0.083	0.039	0.062	0.013
2	0.091	0.136	0.038	0.118	0.066	0.034	0.057	0.012
3	0.237	0.243	0.038	0.197	0.105	0.061	0.099	0.020
4	0.466	0.692	0.054	0.522	0.256	0.167	0.262	0.051
5	0.935	0.705	0.065	0.580	0.349	0.184	0.290	0.058
6	1.420	1.316	0.089	1.755	0.807	0.545	0.879	0.177
7	1.935	1.635	0.113	2.375	1.095	0.735	1.190	0.240
8	2.483	1.741	0.103	2.455	1.110	0.784	1.195	0.245
9	2.983	2.382	0.134	3.535	1.660	1.100	1.770	0.355
10	3.979	3.134	0.147	4.230	2.010	1.330	2.145	0.423
11	0.395	0.397	0.079	0.441	0.224	0.141	0.208	0.046
12	0.851	0.736	0.083	0.992	0.462	0.309	0.484	0.097

Appendix 13-2: SIFT-MS reported concentrations per product ion and related results of offline-HPLC analysis and theoretic calculated concentration for aldehyde calibration.

Calibration Level	Calculated concentration [mg/m³]	result HPLC [mg/m³]	SIFT-MS reported concentration per product ion [mg/m³]				
			$C_3H_5O^+$ [57] / NO^+ / propionaldehyde	$C_3H_5O^+$ [57] / O_2^+ / propionaldehyde	$C_3H_5O^-$ [57] / OH^- / propionaldehyde	$C_3H_6O^+$ [58] / O_2^+ / propionaldehyde	$C_3H_7O^+$ [59] / H_3O^+ / propionaldehyde
1	0.071	0.112	0.204	0.107	0.107	0.154	0.132
2	0.103	0.172	0.142	0.074	0.057	0.080	0.077
3	0.234	0.228	0.186	0.099	0.075	0.092	0.102
4	0.460	0.652	0.488	0.259	0.180	0.208	0.249
5	0.925	0.679	0.543	0.285	0.203	0.226	0.276
6	1.411	1.502	2.175	1.115	0.731	0.855	1.075
7	1.919	1.747	2.925	1.510	0.978	1.140	1.445
8	2.609	1.808	2.955	1.560	1.030	1.205	1.515
9	2.949	2.499	4.355	2.245	1.475	1.695	2.150
10	3.930	3.308	5.170	2.700	1.770	2.025	2.595
11	0.542	0.460	0.677	0.376	0.246	0.300	0.360

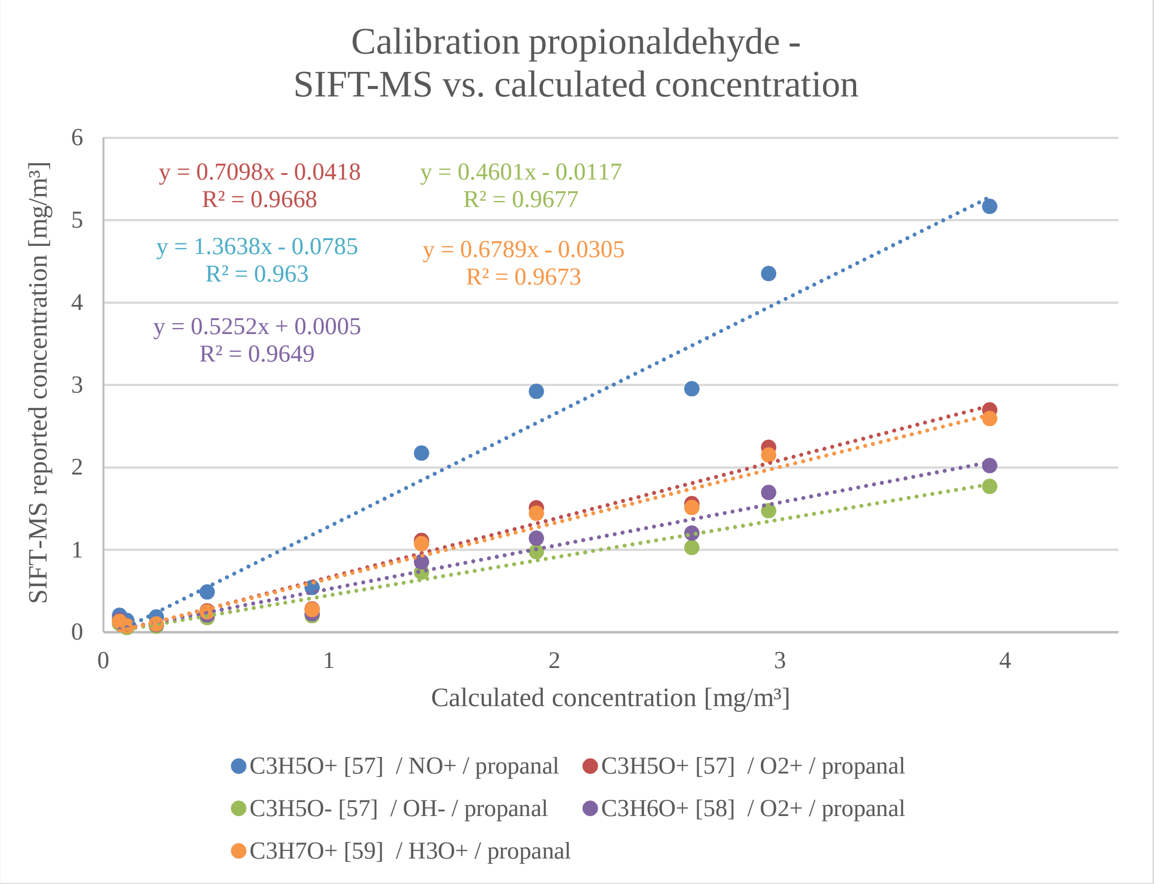
Appendix 13-3: SIFT-MS reported concentrations per product ion and related results of offline-HPLC analysis and theoretic calculated concentration for aldehyde calibration.

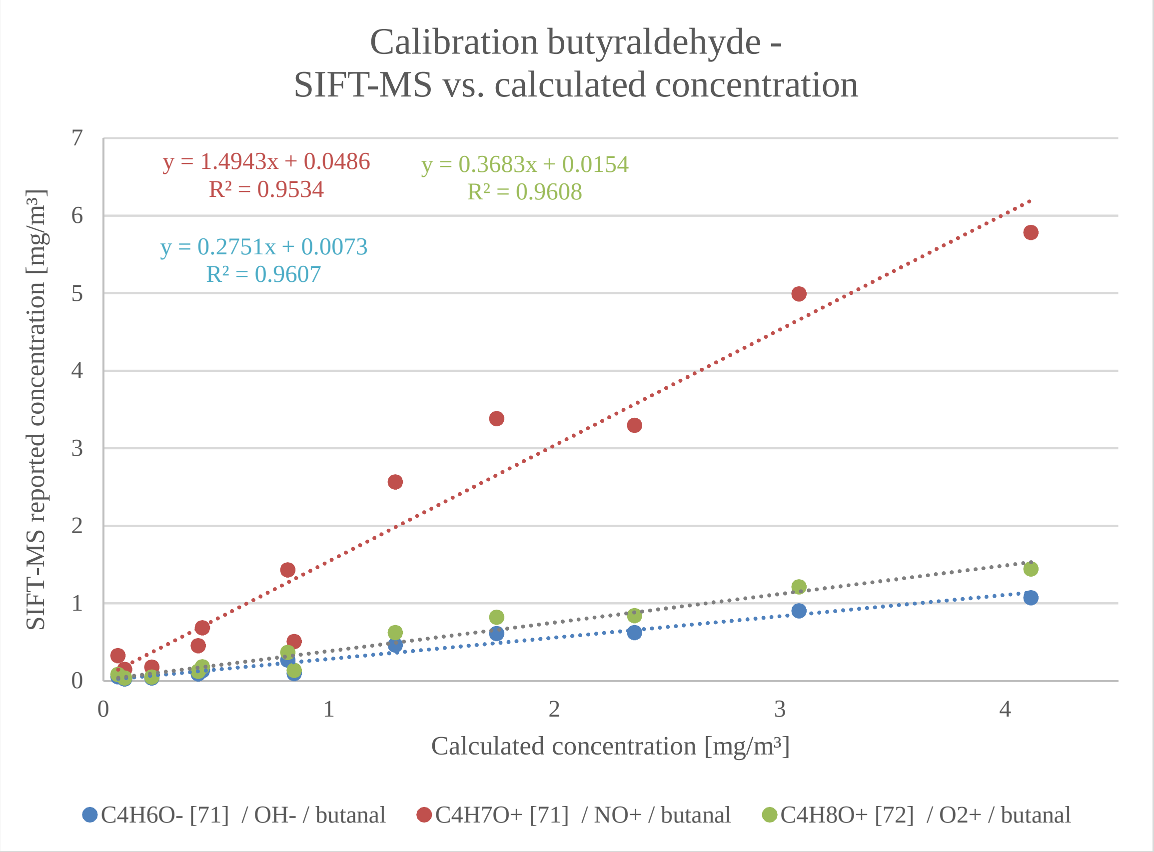
Calibration Level	Calculated concentration [mg/m³]	result HPLC [mg/m³]	SIFT-MS reported concentration per product ion [mg/m³]		
			$C_4H_6O^-$ [71] / OH^- / butyraldehyde	$C_4H_7O^+$ [71] / NO^+ / butyraldehyde	$C_4H_8O^+$ [72] / O_2^+ / butyraldehyde
1	0.065	0.118	0.051	0.325	0.080
2	0.094	0.156	0.024	0.146	0.037
3	0.215	0.146	0.034	0.174	0.048
4	0.420	0.433	0.088	0.450	0.120
5	0.846	0.516	0.094	0.507	0.133
6	1.294	1.390	0.458	2.565	0.620
7	1.744	1.343	0.610	3.380	0.820
8	2.355	1.184	0.623	3.295	0.840
9	3.085	1.875	0.903	4.990	1.210
10	4.114	2.328	1.070	5.780	1.440
11	0.817	0.594	0.264	1.430	0.365
12	0.438	0.367	0.131	0.684	0.178

Appendix 13-4: SIFT-MS reported concentrations per product ion and related results of offline-HPLC analysis and theoretic calculated concentration for aldehyde calibration.

Calibration Level	Temperature permeation oven [°C]	result HPLC [mg/m³]	CH_3O^+ [31] / H_3O^+ / formaldehyde
1	60	0.073	0.038
2	65	0.093	0.032
3	70	0.152	0.040
4	73	0.198	0.054
5	76	0.263	0.069
6	80	0.373	0.163
7	85	0.576	0.228
8	90	0.853	0.311
9	95	1.364	0.486
10	100	2.248	0.704
8.2	90	0.834	0.286
3.2	70	0.152	0.061

Appendix 14: SIFT-MS calibration for aldehydes: SIFT-MS vs. calculated concentration for propionaldehyde and butyraldehyde.





Appendix 15-1: Results of the precision test for validation of the Aldehyde dosage system in combination with real time SIFT-MS analysis. Data evaluation per analyte.

	Acetaldehyde								
	Precision preparation 1			Precision preparation 2			Precision preparation 3		
Calculated concentration [mg/m³]	1.594			1.731			1.746		
SIFT-MS Single measurements after calibration	Conc. [mg/m³]	SD [mg/m³]	RSD [%]	Conc. [mg/m³]	SD [mg/m³]	RSD [%]	Conc. [mg/m³]	SD [mg/m³]	RSD [%]
	1.56	0.056	4	1.41	0.199	14	1.64	0.038	2
	1.58	0.044	3	1.6	0.036	2	1.66	0.037	2
	1.14	0.051	4	1.62	0.100	6	1.63	0.043	3
	1.57	0.033	2	1.64	0.090	5	1.64	0.037	2
	1.39	0.035	3	1.6	0.075	5	1.65	0.037	2
	1.36	0.043	3	1.62	0.120	7	1.62	0.037	2
Average [mg/m³]	1.43			1.62			1.64		
Standard deviation [mg/m³]	0.16			0.01			0.01		
Relative standard deviation [%]	11			0.9			0.8		
Recovery rate [%]	90			93			94		

SD= Standard deviation
RSD= Relative standard deviation

Appendix 15-2: Results of the precision test for validation of the Aldehyde dosage system in combination with real time SIFT-MS analysis. Data evaluation per analyte.

	Propionaldehyde								
	Precision preparation 1			Precision preparation 2			Precision preparation 3		
Calculated concentration [mg/m³]	1.891			1.887			1.785		
SIFT-MS Single measurements after calibration	Conc. [mg/m³]	SD [mg/m³]	RSD [%]	Conc. [mg/m³]	SD [mg/m³]	RSD [%]	Conc. [mg/m³]	SD [mg/m³]	RSD [%]
	1.59	0.025	2	1.62	0.030	2	2.84	0.048	2
	1.57	0.025	2	1.57	0.023	1	2.89	0.068	2
	1.62	0.022	1	1.63	0.041	3	2.91	0.050	2
	1.55	0.026	2	1.65	0.041	3	2.84	0.044	2
	1.62	0.036	2	1.65	0.045	3	2.79	0.050	2
	1.62	0.035	3	1.62	0.053	3	2.81	0.042	2
Average [mg/m³]	1.60			1.62			2.85		
Standard deviation [mg/m³]	0.03			0.03			0.04		
Relative standard deviation [%]	1.7			1.7			1.5		
Recovery rate [%]	84			86			159		

SD= Standard deviation
RSD= Relative standard deviation

Appendix 15-3: Results of the precision test for validation of the aldehyde dosage system in combination with real time SIFT-MS analysis. Data evaluation per analyte.

	Butyraldehyde								
	Precision preparation 1			Precision preparation 2			Precision preparation 3		
Calculated concentration [mg/m³]	1.161			1.159			1.321		
SIFT-MS Single measurements after calibration	Conc. [mg/m³]	SD [mg/m³]	RSD [%]	Conc. [mg/m³]	SD [mg/m³]	RSD [%]	Conc. [mg/m³]	SD [mg/m³]	RSD [%]
	1.11	0.046	4	1.17	0.058	5	1.48	0.045	3
	1.09	0.033	3	1.08	0.031	3	1.51	0.051	3
	1.12	0.027	2	1.13	0.066	6	1.48	0.033	2
	1.08	0.040	4	1.11	0.042	4	1.47	0.046	3
	1.13	0.035	3	1.14	0.048	4	1.47	0.039	3
	1.13	0.036	3	1.1	0.051	5	1.46	0.034	2
Average [mg/m³]	1.11			1.12			1.48		
Standard deviation [mg/m³]	0.02			0.03			0.02		
Relative standard deviation [%]	1.7			2.6			1.1		
Recovery rate [%]	96			97			112		

SD= Standard deviation

RSD= Relative standard deviation

Appendix 15-4: Results of the precision test for validation of the aldehyde dosage system in combination with real time SIFT-MS analysis. Data evaluation per analyte.

	Formaldehyde								
	Precision preparation 1			Precision preparation 2			Precision preparation 3		
Calculated concentration [mg/m^3]	0.415			0.415			0.415		
SIFT-MS Single measurements after calibration	Conc. [mg/m^3]	SD [mg/m^3]	RSD [%]	Conc. [mg/m^3]	SD [mg/m^3]	RSD [%]	Conc. [mg/m^3]	SD [mg/m^3]	RSD [%]
	0.346	0.0114	3	0.345	0.0098	3	0.365	0.0122	3
	0.342	0.0125	4	0.347	0.0127	4	0.371	0.0132	4
	0.338	0.0125	4	0.351	0.0142	4	0.37	0.0142	4
	0.334	0.0116	3	0.355	0.0144	4	0.369	0.0136	4
	0.343	0.0120	4	0.352	0.0118	3	0.376	0.0152	4
	0.343	0.0119	3	0.348	0.0113	3	0.367	0.0152	4
Average [mg/m^3]	0.34			0.35			0.37		
Standard deviation [mg/m^3]	0.004			0.003			0.003		
Relative standard deviation [%]	1.1			1.0			0.9		
Recovery rate [%]	82			84			89		

SD= Standard deviation

RSD= Relative standard deviation

Appendix 16: SIFT-MS online aldehyde analysis. Evaluation of the robustness test.

		Robustness Test 1 – Flow tube 120 °C, Inlet 127 °C		Robustness Test 2 – Flow tube 120 °C, Inlet 113 °C	
	reference value Flow tube 120 °C, Inlet 120 °C	concentration [mg/m³]	% recovery to reference value	concentration [mg/m³]	% recovery to reference value
Acetaldehyde	1.64	1.59	97	1.71	104.3
Butyraldehyde	1.48	1.43	96.4	1.53	103.5
Formaldehyde	0.37	0.35	95.9	0.37	101.2
Propionaldehyde	2.85	2.77	97.1	2.97	104.3

		Robustness Test 3 – Flow tube 113 °C, Inlet 120 °C		Robustness Test 4 – Flow tube 127 °C, Inlet 120 °C	
	reference value Flow tube 120 °C, Inlet 120 °C	concentration [mg/m³]	% recovery to reference value	concentration [mg/m³]	% recovery to reference value
Acetaldehyde	1.67	1.67	100.3	1.54	92.5
Butyraldehyde	1.47	1.47	100.3	1.41	95.9
Formaldehyde	0.36	0.36	100.7	0.35	96
Propionaldehyde	2.95	2.97	100.5	2.87	97.3

9 List of figures

10 List of tables